SECOND VERSION OF COMMENTS FROM STUDENT IN RESPONSE TO EXAMINERS' REPORTS

V 2

July 2012

PhD THESIS REVIEW SHEET for Examiner A	
Document Title: Predicting risk factors of non-contact anterior cruciate ligament injuries during single-leg landing	
Revision: Final	
Author: Nicholas Ali	
Date Submitted:	
Related Docs/Reference: Four examiners reports, Original PhD Thesis and Revised PhD thesis	
Date Evaluated:	

No	Examiner's A Comments and location in Original PhD thesis	Authors' Comment
1	<u>The thesis does not constitute a significant contribution to knowledge and the analysis by the student is not of such quality as to merit publication.</u> Note: although 2 literature reviews are published, neither is in a journal particularly related to the subject matter presented. Neither describes the methodology used to decide on the chosen articles. Neither uses any criterion to evaluate the included articles. As reviews of literature, they are not significant contributions. I would not consider the final three manuscripts (III, IV and V) merit publication	Many thanks for your feedback. For a graduate student to publish a review paper is a significant accomplishment and demonstrates a sound understanding of the literature. The two review papers have been published in peer-reviewed journals in disciplines closely related to the field of biomechanics. The former states that it accepts papers "in all areas of biomedical engineering" and the latter is reviewed by the Canadian Society of Mechanical Engineers and has been publishing since 1972. The problem of a small sample size has been partly remedied by adding several additional subjects to papers 3 and 4. In addition, statistical information was added to prove that the

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	due to, among other things described further on, methodological concerns such as a lack of sufficient subjects (manuscripts III, IV, V). Paper V also lacks model validation (although it is stated many times in the thesis that this has been done) and uses a male musculoskeletal model to represent females (it is simply a scaled down size of model, as pointed out to me by the co-authors on the paper). To my knowledge, this paper has also been rejected outright by the journal it was submitted to, although it is still referred to as submitted in the thesis.	sample size was acceptable. Small sample sizes can yield significant results when the statistical power is high, usually 0.80 is needed. Because of the large differences between the various conditions, a small sample size was shown statistically to be acceptable in papers 3 and 4. Paper 5 only has 6 subjects but this is not uncommon for papers that involve full musculoskeletal models. It is expected that this limitation will not preclude its publication. The MSM modeled utilized for application to single leg landing is the first of its kind in the scientific community, to the best of our knowledge, and therefore should merit publication. As it is known, the gold standard now to validate a MSM is to compare measured and predicted muscle activity as done in the thesis. However, to gain greater confidence in the model, we did many other things. One that is worth reporting in a scholarly publication is the comparison of model predictions to *in-vivo* data in the literature. To facilitate this comparison, the researcher used *in-vivo* studies where body weight and anthropometry of subjects were much higher than those used in the thesis and can likely explain why some of the joint reaction forces do not compare well. To date the data referenced in the thesis are the only data available in the scientific community, of course to the best of our knowledge. The term subject-specific was removed from the paper and term "individualized" was used as suggested. Please see revised paper. You are correct that a male MSM model was used. No female model was available. Since the MSM is individualized for each subject and because there is little difference between male and female anatomy for the lower extremity, this was not deemed a problem. Furthermore, the original accepted thesis proposal did not require developing a female model–a chore that would have taken many years of labour. In papers 3 and 4 a rigid-body model was used (see Attachment B). This model uses classical inverse dynamics analysis and inertial properties that have been individualized to the subjects tested. Furthermore, this model uses cylinders, frusta, and ovoids to represent body segment as shown in Attachment B–a common practice in biomechanics. Paper 5 was submitted and under review at the Annals of Biomedical Engineering before the thesis was submitted. Subsequently, the paper was NOT rejected outright, but was thoroughly reviewed by three reviewers at ABE and deemed unworthy for acceptance. The

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		scientific rationalization for not accepting this paper was provided by all three reviewers and has been revised and submitted to another peer-reviewed journal.
2	1. The work was not done in accordance with established methodology employed by the discipline. (below is a non-exhaustive overview of some of my concerns) Results of the experimental manuscripts are inconclusive and not valid due to lack of sufficient subjects in all three manuscripts. No power analysis was reported but, based on my experience in the discipline, at least 2 to 3 times the number of subjects are required in manuscripts III and IV, likely more would be required for paper V. The paper V purports to evaluate gender differences using musculoskeletal models, however (for example), only three subjects of each gender are evaluated and the model used on both genders is in fact a male model...in other words, the females are in fact treated as height and weight adjusted males. The claim in the manuscript that the model has been validated is not supported by the results. Although the use of a repeated measures ANOVA is questionable in all three experimental manuscripts due to the	This comment was partly answered above. The sample size required for a particular experiment is based on statistical power. Statistical power can be increased in many ways– one of which is increasing sample size. In this thesis the statistical power was increased in many ways and afterwards was tested to show that the sample used in papers 3 and 4 were high. When the difference between the levels of the experimental condition is high as in this thesis (30, 50, 70 cm height, 20, 40, 60 cm distance) a small sample size is acceptable to demonstrate statistical differences. The fact that significant differences were reported confirms again that the sample size was acceptable. Paper V is a modeling effort and experimental data are used to validate and drive the model. There are few MSM studies within the domain of ACL injury biomechanics with over 6 subjects. The MSM model used for this study took over 10 years of research and many PhDs and an enormous amount of money. It was not possible in the scope of this project to create a new one. However, each model was individualized to conform to the anatomy of each subject male or female. It was felt that there are few differences between the lower extremity bones of males and females. Male and female pelvises and thoraxes are very different but since the thesis was mainly concerned with the knee, this should not be a major drawback. From the ANOVA studies conducted, the high F values indicate that we have more subjects that we really need. In fact, for paper 3, we could have easily used 3 subjects and get high F statistics and powers. From work of Cohen 1988, the acceptable powers are above 0.8. There are many studies in the literature where powers below 0.5 are published. However, your point may be valid for PPMC, even though data reported does not substantiate your comment here as well. Recall Pearson correlation is not a robust analytical tool as are ANOVAs. For Pearson correlations, we are trying to develop a regression equation to enable us to make predictions to any other conditions and for any subject. It is harder to get high coefficient of determinations with such small population size and because we had to limit the number of jump heights and distances. Nonetheless, our data do not

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	number of subjects evaluated, it is particularly dubious in paper V where only three subjects are in each group, not to mention that no correction for related measures is considered, nor is the post-hoc analysis described. · The external validity of manuscripts III and IV is limited, as stated by the authors themselves. · The internal and external validity of paper V are limited.	entirely show this. Our data do reveal significant findings for PPMCs for the studies conducted. Paper 5 is a musculoskeletal modeling effort and not an experimental investigation. Its purpose was to develop, validate and apply the models to experimental data to get the internal forces.
3	2. <u>The thesis does not exhibit the candidate's capacity to meet the scholarly standards required. (below is a non-exhaustive overview of some of my concerns)</u> · The methodological concerns noted above indicate that the candidate lacks the scholarly standards from a technical (methodological) point of view. · Information contained in the thesis in misleading since at least two of the declared conference presentations were never presented.	 These concerns have been addressed above. The methods used are common and up-to-date and are regularly used by biomechanists world-wide. The references are included because even though the papers were not presented the papers were published as stated.

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	· Letters from the editors of the journals with manuscripts Under Review are not provided. This is an essential first step since, to my knowledge, at least one of those manuscripts has in fact been rejected outright and this is not noted in the thesis.	Such information is not required in a thesis.
	· The two accepted manuscripts are reviews of literature in journals that are not reflective of the article content and, although accepted, are of limited value due to a less than rigorous or exhaustive methodology which is not coherent with systematic reviews.	Comment is repeated. Biomechanics is a very multidisciplinary field and can only continue to progress with increased synergy between disciplines. Further, as we know,the root of the word biomechanics speaks multidisciplinary as it stems from the application of engineering mechanics to a living body.
	· Manuscripts IV-V lack statistical power, adequate methodological descriptions, and inappropriate use of statistical measures.	Dealt with earlier.
	· The student repeatedly states in this thesis that a lack of multifactorial research exists in the study of ACL injuries yet many of the studies sited are multifactorial in their approaches, in particular those that combine kinematics and kinetics or musculoskeletal models... the student seems to dismiss these in order to justify this thesis, instead of acknowledging what has been done and how it contributes to the field of study and	Please consult figure 2 in both paper 1 and paper 2 to better understand what the authors envision by the multifactorial approach proposed. The multifactorial approach presented is one that uses AI to combine all 5 exiting study approaches in a single unified environment. To date such an approach does not exist in the literature. Further, this type of approach is where research groups are leaning towards.

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	does not seem objective. Then, in the end, the study uses similar methodologies to form his conclusions as the papers previously criticised	
4	3. <u>Even with extensive revision, the thesis would not meet the standards required for the degree.</u> · As a body of work there are too few subjects, weak methodological and statistical approaches and overreaching conclusions beyond the evidence suggested by the results in all three experimental papers. · The two published manuscripts are of limited contribution and published in journals which are not discipline-related.	The thesis has been revised to ensure peer-reviewed publication. Other issues have been dealt with above.
5	The candidate states: *"To the best of the author's knowledge no study to date has investigated gender differences during single-leg landing from increasing vertical landing heights and horizontal landing distances."* Meanwhile, there exists a great body of knowledge about the biomechanics and associated risk factors of single leg landing under various experimental and simulated conditions, including vertical landing heights, for	Thanks for the feedback. This is the first and only study that evaluated both vertical height and horizontal distance during single-leg landing.

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	example.	
6	"Further, there are no MSMs in the scholarly literature that has been developed, validated and applied to single-leg landing in the literature." Untrue, there are… not to mention that the student does not fill this purported void with the thesis.	Thanks for the feedback. It is not currently possible to fully validate MSMs since the data necessary to provide the validation would be too invasive (e.g., strain gauged tendons, ligament etc.). This study has attempted to validate the model using EMGs and comparisons with published *in vivo* studies having similar experimental conditions. This study used the best means currently available.
7	*"Further, the majority of studies in the literature pertaining to single-leg landing do not account for the effects of whole body movement on ACL loading."* Untrue, there are… not to mention that the student does not fill this purported void with the thesis.	Thanks for the feedback. This statement has been reworded.
8	*"In addition, to the author's best knowledge, the current literature demonstrates that there are no proposed multifactorial study approaches aimed at fusing existing non-contact ACL injury study approaches into a single environment using an AI technique."* This statement is unclear since it is unclear what the author is referring to as an AI environment. Two thing are certain: (1) many studies have used multifactorial models and approaches to investigate non-contact ACL injuries; (2) if the candidate refers to the approach he has taken in Paper-V, then it is again untrue	This is an article style thesis. Please provide a study within the domain of ACL injury biomechanics that proposes a study methodology as done in Figure 2 of paper 2. As elucidated in paper 2, there are many AI techniques. The application of a technique to fuse existing ACL injury study approaches in a single environment is novel, we think. A starting point of how to do this can be found in Figure 2 of paper 2. Please consult Attachment A from a renowned researcher in the field of ACL injury biomechanics after reviewing Paper 1 which presents the same method as in paper 2, but with improvements. Keep in mind please the date the papers published by this research group in AJSM and JOB are after Paper 1. Further the statement you quoted above has to do with the "fusion of existing non-contact ACL injury study approaches into a single-environment using an AI technique" which your two points have no bearing on.

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	and others have done this before, whereas if he is referring to some new innovative approach, the candidate has not done it in this body of work nor elucidated what that approach would be.	
9	*"These models are driven by kinematics and external forces."* The candidate is speaking of musculoskeletal models but fails to recognise the body of literature which uses EMG driven models, which are in fact driven by internal forces, as muscles are internal force generators to the system.	The author has referenced in paper 5 studies that use EMG driven musculoskeletal models applied to study ACL injury biomechanics (please see Dr. Lloyd's research group work that was referenced).
10	Very limited since the validity of the studies (both internal and external) is questionable. In particular, a lack of subjects make the results highly speculative and the statistical approaches inappropriate. There is little innovation aside from modifying jump height and distance, and the two reviews of literature are not exhaustive or systematic and seem biased.	This comment was addressed previously.
11	It must also be stated here that paper V uses commercially available software (ANYBODY) to build the model and analyse the data, not a custom model developed by the student. This is not clear in the thesis.	Please see section titled "Model development and validation" of paper 5 where your concerns were addressed. The model was taken out of the repository and individualized to each subject. This is an approach that is often used in MSM research. The model used was "individualized" for each subject by using body dimensions unique to each subject, thus each data file can be said to be customized.
12	Paper 1:	Thanks for the feedback. It was not the intention of this work to gravitate towards any

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	. The methodology described for the initial review of the literature seems initially exhaustive, however when I used one of the 4 search terms provided by the authors I turned up 3743 articles whereas the authors found 813 articles total; furthermore no criterion for triage down to the 147 articles cited is given by the authors. Considering the strong focus on modeling in the paper, at least one search term should include the word model or simulation, for example.	particular ACL injury study approach, we presented what we found. If there is a lending to any one study approach, this may be a reflection of preference of methods employed in the literature. .Finally the most significant 813 articles were reviewed for this thesis.
13	Paper 1: . One example of a lack of depth to the discussion: *"Mathematical programming and the Monte Carlo method (Blankevoort and Huiskes, 1996; McLean et al., 2003) are the current often used optimization approaches employed to study ACL mechanics. Although both mathematical programming and Monte Carlo methods have demonstrated their usefulness and effectiveness as a research tool, there are much more advanced and robust AI techniques; namely, taboo search, simulated annealing, genetic algorithms, and artificial neural networks."* In fact, "simulated annealing" is currently one of the most popular and widespread methods in musculoskeletal modeling...	The focus of paper 1 and paper 2 is in the domain of ACL injury biomechanics and overcoming existing barriers to our understanding of the mechanisms and risk factors to ACL injury and not to the entire domain of biomechanics or musculoskeletal modeling. We do accept in the paper that simulated annealing has been applied to ACL injury study by one research group. At the time of writing this paper, to the authors' best knowledge, the only application – referenced in the thesis – of an AI technique to ACL injury biomechanics was by McLean et al. (Clin Biomech. 2004 and 2008). In the earlier paper (Mclean et al. 2004) only the word simulated annealing (SA) is mentioned. How the technique is applied to this study is not provided. Regardless, the authors use SA to minimize the difference (errors) between predicted and baseline muscle simulation data. Minimizing the difference in errors using an iterative search technique is common in mathematics and has nothing to do with the study methodology proposed in paper 1 and paper 2.

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14	Paper II: It is not quite clear if this paper is a review of literature or opinion-piece on how to investigate ACL injury. To me, it is more of an opinion piece and is more suited to be in a thesis discussion then as a publication since it lacks objectivity.	The paper has been published so further discussion of its merits seem irrelevant.
15	Paper II: It is not clear why the authors would chose this journal as it does not seem to be related to the field being investigated.	The paper has already been published.
16	Paper II: Similar concerns with regards to the approach and criterion used to select papers as paper 1 above.	The paper has already been published.
17	Paper II: This paper would serve as an introduction to the thesis, but in my opinion is not an in depth review.	The paper has already been published.
18	*Note that while I believe it is a good idea to try and publish one's thesis, papers one and two seem to be the review of literature portion of the thesis as opposed to original scientific contributions to the literature.*	Paper 1 and Paper 2 are original scientific contributions to the literature and has already been published.

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19	Manuscripts III and IV: There is a lack of subjects, putting the statistical analysis and validity in doubt. I believe that this statement by the authors is worth noting *"this study is limited by a small sample size; hence our results may not be representative of the general population and may not be conclusive. While we cannot conclude the general male population would exhibit sagittal plane body kinematics, knee power, and knee work as determine in our study for single-leg landings, we were able to show that the relationships found have a good fit in terms of r2 and p values for the six subjects tested."* The r-square and p values are questionable since there were not enough subjects to perform these tests in the first place...as a PhD thesis, this is unacceptable. These two manuscripts are better described as pilot projects or incomplete projects.	As addressed above and in the revised MS statistical was acceptable for the ANOVA. The r-values were used to demonstrate only that there was a linear increase with most of the subjects as the experimental conditions increased in difficulty.
20	Manuscripts III and IV: . Even if one considers the correlation values reported, the relatively low levels of correlation make conclusions difficult to support (a statistically significant correlation does not necessarily mean an important one...)	Be aware that adding subjects to the pool does not necessary guarantee one an increase in correlation coefficients or powers given the variability to be expected when testing humans.
21	Manuscripts III and IV:	This is true. Paper 1 and paper 2 are separate pieces of work. The lack of funds, resources, skill sets, and support has forced the candidate not to pursue the development of the

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	. The emphasis in the two reviews of literature is to avoid a reductionist approach when studying the ACL injury, yet these manuscripts do exactly that.	methodology. The development of such a methodology requires a research group with software, computing capability, and disparate skill sets, which was and still is lacking. The new research paradigm proposed is something that is absent from the scholarly literature. Regardless, paper 1 and paper 2 are reviews of the literature that exposes many gaps in knowledge in the field of ACL injury biomechanics, steers future research direction, and provides a possible way to address these gaps via the new research methodology proposed. Hence, the review of the literature does not center on this new proposed approach, but non-contact ACL injury.
22	Manuscripts III and IV: . It is unclear if the subjects from paper III were used in paper IV and this should be stated.	This has been amended to make clear in the thesis.
23	Manuscripts III and IV: . A table containing the dependant variables is not clear *"various selected dependant variables"* is the only information given.	This has been amended to provide these tables in the thesis.
24	Manuscripts III and IV: .No consideration of the inter-dependence of the selected variables is given and no correction of the probability coefficient is considered for these variables	The interdependences of various dependent variables on risk predictor is provided given the aim is to assess risk of injury. Further, the effect of an independent variable on selected dependent variables was provided. A sensitivity study may provide more information, but this approach provides a limited view of the problem as mentioned in paper 1.
25	. Given paper IV, paper III seems redundant.	. Paper 4 builds on Paper 3 by adding the effect of gender and a much larger study population. As per paper 3 "Future studies by the authors will endeavor to employ a larger sample size as well as to account for the effect of gender during single-leg landings from varying heights and distances."
26	Manuscript V:	Repeated comment. See comments above. Further, paper 5 is a modeling effort with the aim

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	·Too few subjects (3 males and 3 females) to extract meaningful conclusions. Similar to manuscripts III and IV, this manuscript is a good beginning, but not and end product.	of developing, validating and then applying MSMs to single-leg landings. This type of study and the data reported are absent from the literature and hence is deemed novel.
27	Manuscript V: . There is a lack of model validation: the authors somehow conclude that the musculoskeletal model is valid based on EMG activations which are not reflective of the predicted model-driven activations, with no objective comparisons...this makes no sense to me.	The on/off timing curve provides this objective comparison. Further to this, we have added average correlation coefficients for the 8 muscles measured with model predictions. As well, we have provided comparisons of *in vivo* joint reaction forces and moments with model predictions to aid model validation.
28	Manuscript V: The model used in this paper is not novel nor is it developed by the candidate: it is an application of a musculoskeletal model from the ANYBODY Software repertoire, which requires the user of that model to adjust the model to the input data.	As was stated in the paper 5: "The development of a MSM from the ground up is a very time consuming and complex endeavor. To mitigate these challenges, the AnyBody research group has embraced a philosophy of creating a model repository and sharing it with the public. The GaitFullBody MSM was extracted from the repository and individualized for each subject." The musculoskeletal model used for this study is the most heavily worked on and verified model in the AnyBody modeling repository hence its usage for this thesis. The development of such a model from the ground up is an enormous undertaking. Regardless, the co-authors of this paper can assure you that the modeling effort to get this model to work for application to single-leg landing was over six months of work with the software developers themselves (co-authors in this paper) in Denmark. The novelty is the application of the model to single-leg landing over increasing vertical heights and horizontal distances which has never been reported in the literature. Further, a MSM investigating single-leg landings does not exist in the literature hence the novelty. To achieve stability for MSMs applied to high acceleration tasks such as for single-leg landings is no trivial task and has never before been conducted.
29	Manuscript V: The model used for the female subjects is a scaled version of the male model, not a gender-specific model. As such, it cannot	Addressed previously. Please note, the purpose of the paper is not to investigate anatomical differences.

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	take into account physiological and anatomical differences between the sexes, even though the purpose of the paper is to evaluate these things.	
30	.The statistical analysis of the results is questionable due to the small sample sizes in all manuscripts.	See comments above.
31	. The validity of the model used in paper V is not established; the use of a male musculoskeletal model to represent females is questionable, in particular given the anatomical and neuromuscular sex-related differences highlighted by the candidate, for example.	.One may argue that there is no difference is lower extremity anatomy below the pelvis between genders. This problem was not addressed nor required by the committee that reviewed the thesis proposal so is beyond the scope of the current thesis.
32	.The value of the conclusions was accurately put into doubt by the candidates own statements regarding a lack of sample size for manuscripts III and IV.	Addressed above.
33	.The value of the conclusions for paper V are in doubt due to a lack of sample size and the above mentioned lack of model validation and use of a male model to represent females.	Addressed above.

PhD THESIS REVIEW SHEET for Examiner B	
Document Title: Predicting risk factors of non-contact anterior cruciate ligament injuries during single-leg landing	
Revision: Final	
Author: Nicholas Ali	
Date Submitted:	
Related Docs/Reference: Four examiners reports, Original PhD Thesis and Revised PhD thesis	
Date Evaluated:	

Examiner B

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1	. ***Lack of anatomical description of the knee structures and the role of the ACL within this overall structure*** – Given the thesis topic, early in the thesis it would be appropriate to include a detailed description of the knee anatomy and function, including clear diagrams of the ACL, its location, and its role within the complete milieu of ligaments, muscles, cartilage and bones that form the knee structure. This description (and accompanying diagrams) should make very clear why jumping from various heights and distances might be expected to cause ACL injuries, thereby helping to build the rationale for the	. Thanks for the feedback. I have endeavored to add material to the introductory chapter to address your concerns.

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	experimental work to follow.	
2	. ***Duplication of review of literature material in papers 1 and 2*** – Although I understand that papers 1 and 2 were written for separate publication in academic journals, there is much overlap between the 2 chapters. From the perspective of the thesis document, I think the review of literature would be much better served if written as a single chapter. The 2 submitted papers could be included as Appendix material.	. Thanks for the feedback. In paper 1, to rationalize why new research methodologies are required, the challenges to understanding the mechanisms and risk factors to non-contact ACL injuries are presented. Further, the authors proposed a possible methodology to address many of these challenges. For paper 2, the goal is to bring awareness of two optimization approaches, i.e. OR and AI. The authors provide rationalization of why AI is better suited of the two approaches to address the challenges of non-contact ACL injury. But, what are these challenges. These challenges as presented in paper 1 had to be repeated to make paper 2 all encompassing, a standalone document and complete. So in order to justify the use of an OR or AI technique, the authors first needed to tell the story about the problem. The problem is why we still do not know how and why non-contact ACL injury occurs. Hence, there are repeats in the background information on the challenges to understanding non-contact ACL injury in papers 1 and 2. The authors presented tools available in the optimization world from both OR and AI communities that can possibly address these challenges. The authors went on to show why AI approaches may be appropriate to tackle the problem of how and why the ACL gets injured. This sort of proposed study methodology was absent from the literature, to the best of our knowledge.
3	***Possible lack of awareness concerning use of optimization techniques such as simulated annealing and genetic algorithms in the biomechanics literature*** – While reading the Introduction and paper 1, I was intrigued by the author's contention that present study approaches are inadequate and that he was proposing to use new state-of-the-art artificial intelligence (AI) tools and techniques. However,	. Thanks for the feedback. Please note that paper 1 and paper 2 are focused on the domain of ACL injury biomechanics and NOT the entire field of biomechanics. If we are to consider the entire field of biomechanics your claim may be accurate. At the time of writing the 2nd paper and to the author's best knowledge the only application – referenced in the thesis – of an AI technique to ACL injury biomechanics was by McLean et al. (Clin Biomech. 2004 and 2008). In the earlier paper (Mclean et al. 2004) only the word simulated annealing (SA) is mentioned. How the technique is applied to this study is not provided. Regardless, the authors use SA to minimize the difference (errors) between predicted and baseline muscle simulation data. Minimizing

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	much of the text was vague and lacking details. It was not until near the end of paper 1 (page 45) that I discovered that the AI tools include optimization techniques such as simulated annealing and genetic algorithms. Although the author may (or may not) be correct in saying that there are no non-contact ACL injury papers that use these techniques, simulated annealing is a commonly used optimization technique in the biomechanics literature, and has been for over 10 years. The tone and vagueness of the author's writing implies that these are new techniques that are at the heart of a new, integrated study approach that is better than those presently used in biomechanics research. I disagree, and wonder if this is poor writing, a difference in terminology associated with the author's background training, or is the author unaware that these techniques are commonly used in biomechanics research?	the difference in errors using an iterative search technique is a common practice in mathematics and has nothing to do with the study methodology proposed in paper 1 and paper 2. In a later study, McLean et al. (Clin. Biomech. 23, 2008, 926-936) provided more details into the application of SA to ACL injury risk prediction. However, the application of this technique by McLean et al. is exactly the same as mentioned above, and therefore is not as what is proposed in paper 1 or paper 2. Further, one would not be able to use this study to implement their own SA method given problem in McLean et al.'s 2008 paper is ill defined. In McLean et al. 2008 study the authors mention the objective function and variables but no constraints or constraints approach. Further, the authors used a fixed number of iterations as opposed to terminating the program against some test of optimality. Nonetheless, given McLean et al. 2008 applies SA to minimize errors between predicted and baseline muscle simulation data, it has no relevance to work presented in our paper 1 and 2. In this vain, we would like to ask that you highlight to us please the use of AI technique to the field of ACL injury biomechanics. In our paper # 1, the novelty is not in AI or OR techniques that have been existing for many decades, but in the application and how to apply an AI technique to address the barriers to our understanding non-contact ACL injury mechanics. Paper 1 presents a way using AI to fuse existing ACL injury study approaches into a single unified environment to better understand how and why the ACL gets injured. We kindly ask the examiner to show us a research paper that presents a paradigm that uses AI to fuse existing study approaches into a single environment with the objective to predict ACL injury. Paper 2 provides more details, awareness, and possible techniques from AI and OR communities that may be utilized in ACL injury research. Again, here the paper is focused on application of AI and OR to the study of non-contact ACL injury biomechanics, but not the entire field of biomechanics. What is exciting about paper 2 is that the research community is slowly beginning to realize that new research methodologies are required to understand ACL injury mechanics. These new approaches perhaps need to borrow from each approach given each approach on its own

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		has its own strengths but also limited in its ability to fully capture factors implicated to increase the likelihood of ACL injuries. So, the question then is how can we capitalize on the strengths of existing study approaches so we can more comprehensively and completely capture the problem of ACL injury mechanics. One possible tool to do this is optimization, more specifically AI. The authors also present a refined way to do this in the paper 2. You are correct that AI was applied to the field of biomechanics for decades, but not to non-contact ACL injury biomechanics, which is the focus of this thesis and both papers 1 and 2.
4	. ***Inconsistency between "gap" study described in papers 1 and 2 with subsequent experimental papers 3, 4, 5*** – in papers 1 and 2, the author's viewpoint on currently used study approaches is clear. A main point of both papers 1 and 2 is that ACL injuries are multi-faceted, and current approaches that try to elucidate the role of a single risk factor are inadequate. In paper 2, the author describes a better approach that would incorporate multiple risk factors within a unified research approach. Because these papers formed the literature review that was to identify "gaps" in the literature and therefore provide the rationale for the author's doctoral work, I was expecting that the subsequent experimental and modeling efforts would follow this multi-faceted approach. However, papers 3 and 4	. The lack of funds, resources, skill sets, and support has forced the candidate not to pursue the development of the methodology. The development of such a methodology requires a research group with software, computing capability, and skill sets which was and still are lacking. To make Paper 1 and Paper 2 more easily publishable, the authors felt the need to add the element of a new research paradigm. This new research paradigm is something that is absent from the literature. You are correct that the existing approaches presently used in the biomechanics community were used in our research too, but this is within the limits of what can be done within the facility and resources available to the student. Regardless, paper 1 and paper 2 are reviews of the literature that expose many gaps in knowledge in the field of ACL injury biomechanics, and a possible way to address these gaps is the new research methodology proposed. The new research methodology was added to the publication to assist getting the paper published and arguably one of the most significantly contribution of this thesis.

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	use the typical biomechanics approach that the author had criticized in papers 1 and 2. Even in paper 5 where the author describes a MSM, it is used to further analyse the same conditions (and same experimental data?) as in paper 4, and not in the manner described in papers 1 and 2.	
5	. ***Lack of lateral and medial jump directions in papers 3, 4, 5*** - It is clear from the literature that one situation that puts the ACL at risk is movements that include a component in the medial-lateral direction in addition to anterior-posterior motion, such as "cutting" maneuvers during running. Why did the author choose to vary vertical height and anterior-posterior distance in the landing conditions, but not medial-lateral distance?	. There is no consensus in the biomechanics community that side-step cutting is a non-contact ACL injury mechanism (Quatman and Hewett, Br. J Sports Med, 43, 2009; Boden, Orthopaedics, 23, 2000, Olsen, Am J Sports Med, 32, 2004). The answers to the following questions are also not given yet in biomechanics community: Does valgus collapse cause ACL injury or valgus collapse happens as a result of the ACL being injured? At the vertical heights and horizontal distances studied, we conducted lateral jumps but did not include these in our studies given at some of the heights and distances studied some subjects were not comfortable performing these tasks. In addition, it proved challenging to ask subjects to jump on a single-leg from all these heights and distances so many times. That's why we did not include this way of jumping in our study. Medial jumps placed the subjects at great risk of injury due to inability to regain balance with this type of jumps, so it was not included in experiment. Further, medial and lateral jumps will likely lead to pronounced medial and lateral compartment forces which may lead to internal rotation of the tibia on the femur, which can dramatically increase the strain on the ACL (Markolk KL et al., 2005). In addition medial landings were seen as dangerous tasks for our study protocol given the increased risk of inducing high internal tibial rotations during this form of landing. Based on others' results, it is known that internal tibial rotations can increase ACL strain

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		(Arms SW et al. 1984, Berns GS et al. 1993) and also ACL force (Markolf KL 2005). It should also be noted that for this type of movement even though it is sagittal plane dominant, the abduction moment does play a role given the proximal femur is inherently abducted. The following papers looked at knee ab/ad for single-leg landings (Lawrence RK, Clin. Biomech. 23,6,2008; Nagano Y. et al., The Knee, 14, 2007; and Russel KA, et al., J. Athl. Training, 14,2,2006) and for double-leg landing (Decker MJ et al. Clin. Biomech. 18,7, 2003, Kernosek TW, Med.Sci. Sports Ex. 37,6, 2006, Chappel JD, Am. J. Sports. Med, 30, 2, 2002).
6	***.Incomplete description of results in papers 3, 4, 5*** - The landing experiments that form the basis for papers 3, 4 and 5 will have produced a wealth of kinematic and kinetic data that describe the time-varying changes that occur as subjects prepare and execute their landing. However, the author has chosen to describe and present very little of these data. In the first of these papers (chapter 4), there are no time series data reported at all, making it difficult for the reader to appreciate how the subjects reacted to the different landing conditions. The only data reported are peak vertical and posterior GRF, plus values for some joint variables at	. Thanks for the feedback. Yes, there is a wealth of kinematic and kinetic data but selecting as well as processing the right data to support your objectives and arguments is a demanding and challenging task. The authors provided only the data in the journals to convey the objectives of each paper. So, given this is an article style thesis one needs to be selective in what best conveys the aims and hypotheses of the paper. Also many journals have restrictions on the number of figures and tables to include (e.g., Annals of Biomechanics and Biomedical Engineering maximum is 8), so even though there is a wealth of data it does not add more knowledge than what the authors already reported. So we chose to report data that best conveyed our objectives. We have added many time history plots to the thesis as per your suggestion. . The thesis focus is on risk of ACL injury. In the literature the way to establish risk is as done in this thesis, that is, a single point is used to establish study variables (dependent variables) implicated to cause injuries, for example, initial contact, peak VGRF, peak PTASF, peak knee flexion,

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	the time of these peak GRF occurrences. One variable was knee joint work, which is calculated by integrating the knee joint power curve over some time of interest (which is not described). How are we to interpret these single value data? Do these variables also reach their peak at the time of peak VGRF or PGRF? It is inappropriate to use that single value to represent joint motion during landing execution. For example, having a knee flexion value of -33 degrees (Table 1, page 94) at the time of peak VGRF does NOT indicate the degree of knee flexion during the landing phase; it is only one measurement from a time series of knee flexion angles. The date form the basis for correlations with VGRF (Table 2), and the correlations are then interpreted with statements such as (page 96) *"Our results showed that at increasing vertical heights, knee flexion was not correlated to peak VGRF and therefore may have little potential for reducing the risk of non-contact ACL injuries during single-leg landings."* This is incorrect, as the author has not assessed the amount of knee flexion in each landing, only the knee flexion angle that occurred at peak VGRF. This "single	etc. For example, the following quotes taken from scholarly literature (keep in mind please that none of these studies measured ACL strain or modeled the ACL): a. "The results of this study show that the peak knee extension moment and peak proximal tibia anterior shear force are significantly correlated to each other. This result provides further support to the notion that proximal tibia anterior shear force and knee extension moment are indicators of ACL loading." (Yu B, 2006) b. "The results of this study further show that the magnitude of the peak proximal tibia anterior shear force and knee extension moments during landing of the stop-jump task are significantly correlated to corresponding peak ground reaction forces, especially the corresponding peak posterior ground reaction force. These results suggest that the peak ground reaction forces can be used to predict ACL loading conditions in future research and practice." (Yu B, 2006) c. "Hewett et al (2005) have shown that women tend to land with higher knee abduction moments (valgus torques), which are significant predictors of future ACL injury risk." (Boden B, 2009) d. "In the present study, subjects with strong hip external rotators demonstrated significantly lower VGRF during single-leg landing. This increased hip external rotator strength may provide insight as to why neuromuscular training studies have also been shown to decrease VGRF during landing (Hewett et al., 1999). The present study suggests that by improving proximal hip strength and thereby avoiding these poor landing styles the risk of ACL injuries to athletes could be lessened." (Lawrence 2008) e. "Landing with a more extended knee angle decreases the ability of the hamstring muscles to prevent anterior tibial translation, thereby increasing the risk of ACL injury. (Fagenbaum and Darling 2003)

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	value at time of peak GRF" is repeated in papers 4 and 5, and can lead to incorrect conclusions on any variable assessed. There are some time series data shown in papers 4 and 5, and some bar charts of gender-specific muscle forces in paper 5. In my opinion, more of these data should be reported in all 3 experimental papers.	f. We expected that women would land with more extended knees, potentially predisposing them to a greater incidence of ACL injuries. Arendt E. and Dick, R. Am. J. Sports. Med. 1995, Gomez et al. Am. J. Sports. Med.,1996). g. Limiting the valgus position of the knee during a single-leg landing could reduce strain on the ACL and in turn reduce the number of non-contact ACL injuries. (Russel 2006) i. "The finding of increase peak VGRFs in females is important as a previous prospective study of ACL injury risk demonstrated that athletes who went on to subsequently tear their ACL had 20% greater VGRF during a drop landing." (Schmitz et al., Clin Biomech, 2007) j. "Without sufficient strength available to decelerate the body by the eccentric quadriceps mechanism, it seems that the females land in a more extended knee position and tend to maintain this extended position subsequent to ground contact rather than absorbing the impact with controlled knee flexion. This knee extended position, combined with internal hip rotation, makes females vulnerable for anterior cruciate ligament loading." (Lephart et al. Clin. Orthop. Rel. Research, 2001). Note all of these studies are done in-vitro. In none of these studies was the ACL strain or force directly measured. In most if not all of these studies the risk of ACL injury was investigated. To the authors' best knowledge, this is the norm and has been the norm for the last two decades. Now, if you randomly take any reference from this thesis in the domain of ACL injury biomechanics, you will observe the similar style inferences being made. The authors would venture to argue the same argument can be made about any other injury mechanism studied in the domain of ACL injury biomechanics.

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		We have added many time histories plots for many dependent variables. Also please keep in mind that many journals have limits on number of figures and tables that can be included. So, the observation of body kinematics, muscle and joint forces, and external forces as well as their interactions may help us determine how the body responds to safely reduce the impact forces. Hence, ankle, knee, hip or trunk flexion at time of peak VGRF with increased task demand may inform us as to how the body responds to these demands to attenuate impact forces and subsequently risk of ACL injury.
7	***Incorrect interpretation of at least some correlation data in papers 3, 4, 5*** - At least some of the correlation data in these chapters have been interpreted incorrectly. For example, in paper 3, peak PGRF data are plotted as a function of horizontal distance jumped in Figure 2, page 95. Notice that on the vertical axis, the PGRF values are all negative, which is an indication that the posterior direction has been assigned to the negative, while the anterior direction is positive. Further, notice that as you scan across the graph from lower horizontal distances (30 cm) to higher ones (50 and then 70 cm), the PGRF values INCREASE in magnitude (from ~-0.6 to -0.8 for the mean).	. Thanks for the feedback. Your comment of correlation between PGRF and horizontal distance is correct. We have corrected this as well as rechecked all other correlations to ensure accuracy. Using a lumped mass approach and basic mechanics will confirm the accuracy of the above statements (see attachment B). Landing as seen in this thesis is 3D, includes multisegment kinematics, and most importantly includes the muscles that all work together to dampen the loads on impact. How the body dampens these impact loads is one of the mandates of this thesis. I think that just considering a lumped mass approach for single-leg landing then employing Newton's law is not a true strategy. As well, our system is not closed with respect to the momentum and energy transfer. Thus, just simply using a rough, say, conservation of linear momentum between the beginning and end of a landing trial does not seem to be correct.

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	Because of the negative values assigned to the posterior direction, this forms a negative slope on the graph, and the author reports this negative correlation as *"The other significant finding of this study…"* (page 93, in Results). However, the author mis-interprets this negative slope when he states on page 97 *"Our results …… there will be a REDUCTION in peak PGRFs for landings performed at increased landing distance"*. This is particularly troublesome for the GRF data, as this statement of reduced horizontal force with increased jumping distance runs contrary to Newtonian physics: with increased horizontal jump distance, the horizontal take-off and landing velocities MUST increase, and the horizontal landing impulse (force X time; area under the force-time curve) MUST increase to bring the horizontal velocity to zero upon landing. One would expect the peak PGRF values to also increase in magnitude (as they do), although it is possible for the impulse to increase but not the peak PGRF. This level of mechanics knowledge should be well within the capability of a doctoral student in biomechanics. The author should carefully check	

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	the interpretation of ALL correlations, especially ones that include positive or negative signs that indicate direction (e.g. force vector components, joint angular velocities, joint moments).	
8	*.Incomplete description of subject population(s) in papers 3, 4, 5* - In paper 3, there are 6 male subjects. In paper 4, there are 6 male subjects and 5 female subjects. Are these the same male subjects in both studies? Are the data from paper 3 and 4 from the same experimental data collection, or form 2 different data collections? In paper 5, there are 3 male and 3 female subjects. Are these a subset of the subjects in papers 3 and 4? Why is EMG data only reported for the 6 subjects in paper 5? If any of the subjects / data are the same in the 3 papers, this should be noted when describing the subjects in papers 4 and 5.	. Are these the same male subjects in both studies? Yes Are these the same male subjects in both studies? Yes Are the data from paper 3 and 4 from the same experimental data collection, or form 2 different data collections? Yes, same experimental data collection. In paper 5, there are 3 male and 3 female subjects. Are these a subset of the subjects in papers 3 and 4? The 6 subjects are a subset of the subjects in papers 4. Why is EMG data only reported for the 6 subjects in paper 5? EMG data was recorded for the purpose of MSM validation. If any of the subjects / data are the same in the

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		3 papers, this should be noted when describing the subjects in papers 4 and 5. . This has been done. Be aware please, however, this is an article style thesis and these manuscripts are very separate papers with different objectives, hypothesis and methods.
9	***Poor statistical power in papers 3, 4, 5 due to small subject numbers*** – In the 1970s and 1980s, it was normal for biomechanics studies to have relatively few subjects due to the tedious and time consuming data analysis procedures (cinefilm methods with hand digitization, force plate data needed to be carefully synchronized, and all data reduction and analysis performed with custom written software). However, in the past 20 years we have seen the advent of automated motion capture systems which seamlessly integrate time synchronized kinematic, kinetic and EMG data, and off-the-shelf 3D analysis software (e.g. Visual 3D) and MSM software (e.g., OpenSim, AnyBody). With this improvement in data handling we have seen larger numbers of subjects in biomechanics studies, which brings greater statistical power. Why are so few subjects used in the studies described in papers 3 and 4, and particularly in paper 5? Did the	. From the ANOVA studies conducted the high F values indicate that we have more subjects that we really need. In fact for paper 3, we could have easily used 3 subjects and get high F statistics and powers. From work of Cohen et al. (1988) acceptable powers are assumed to be above 0.8. There are many studies in the literature where powers below 0.5 are published. However, your point may be valid for PPMC even though data reported does not substantiate your comment here as well. Recall Pearson correlation is not a robust analytical tool as ANOVAs. For Pearson correlations, we are trying to develop a regression equation to enable us to make predictions to any other conditions and for any subject. It is harder to get high coefficient of determinations with such small population size. Nonetheless, our data does not entirely show this. Our data does reveal significant findings for PPMCs for studies conducted. Paper 5 is a musculoskeletal modeling effort and not experimental effort whose purpose was to develop, validate and apply the models to experimental data to get the internal forces. We are still to see a MSM study applied to non-contact ACL injury mechanics that employ more than 6 subjects. We did not perform *a priori* power analysis.

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	author perform a statistical power test *a priori* that suggested such low subject numbers?	
10	***.Incomplete description of MSM in paper 5*** - In paper 5, the author uses subject-specific MSMs to predict the forces in internal body tissues. However, the model is not described in sufficient detail, with only general statements used such as *"The GaitFullBody MSM was … individualized for each subject"* and *"… the model is made subject-specific by employing a length mass fat scaling algorithm that uses the anthropometric data measured for each subject to scale the MSM"*. What data are used as inputs to the model? What anthropometric measures were used in the scaling? How many muscle models are included in the model? Are differences in individual subject joint strengths (measured with a dynamometer), or muscle morphology (from MRI or ultrasound) included in the subject-specific models? Were the muscle model force-velocity, force-length and elastic characteristics subject-specific? Was the force plate data used as input to the model, or did the model include a foot - floor interface that would generate GRFs as model	. Thanks for the feedback. The paper was changed to address all your concerns so as to better describe the model. Are differences in individual subject joint strengths (measured with a dynamometer), or muscle morphology (from MRI or ultrasound) included in the subject-specific models? .The answer is no. A simple muscle model was used that assume constant strength. Was the force plate data used as input to the model, or did the model include a foot - floor interface that would generate GRFs as model outputs? . Force plate and kinematic data from experiment were used as inputs to the musculoskeletal model. Was there an objective function that was optimized? Were there constraints on the solution? How were they imposed, as "hard constraints" or as penalty terms in the objective function? Which optimization algorithm was used (e.g. simulated annealing)? There are two modelling process and models in the development of the musculoskeletal model. First model is a kinematic model that matches the motion capture marker data from experiments with the rigid body model in

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	outputs? How did the MSM generate its muscle model activity timing as seen in Figure 2? Was there an objective function that was optimized? Were there constraints on the solution? How were they imposed, as "hard constraints" or as penalty terms in the objective function? Which optimization algorithm was used (e.g. simulated annealing)? A much more complete description of the MSM and how it was tailored to each subject is needed.	AnyBody "the man". This is a kinematic optimization process whose objective function is geared towards minimizing the distance between markers from experiment and model "the man". In doing this, the man becomes scaled to the person anthropometry in experiment. The optimization process stops when there is an acceptable level of error that is set by the user. For further details of the optimization routine (by no means AI based) please see (Andersen et al. 2009). The Second model is an inverse dynamics model. This model uses a min/max objective function (Rasmussen et al. 2001). The basic optimality assumption is that "the body attempts to use its muscles in such a way that fatigue is postponed as far as possible". Hence in our optimization problem we would minimize the maximum muscle activity subject to equilibrium constraints and positive muscle force constraint (muscles can only pull). AI methods are not employed in AnyBody. The software uses Newton Raphson methods for the kinematic problem. It then uses the golden section method for inverse dynamics. How did the MSM generate its muscle model activity timing as seen in Figure 2? Details of the mathematical and mechanical methods of the AMS software are described in the literature and referenced in the paper. Please consult the following references: (Damsgaard et al. 2006; Rasmussen et al. 2001)
11	***.Use of gait data in model "validation"*** - In paper 5, the author describes the use of *"gait data collected during our study"* for purposes of validation. What gait data were collected (none was described in the experimental procedures)? Was it for the same	. Thanks for the feedback. The details of the walking gait trials collected from the same subjects prior to the single-leg landing tasks was added to the thesis. Yes, the same subjects that performed the single-leg landing task performed the walking gait task. The subjects were asked to walk naturally without accelerating or decelerating while dominant leg strikes the force plate.

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	subjects? Running? Walking? What was the progression speed? Was the gait at constant speed, or were the subjects accelerating or decelerating? Were the foot - floor interface parameters the same for gait as in single-leg landing? Should they be? And even if the gait model results were compared to literature values as in Table 1, how do we know the MSM will be valid in an impact situation with sudden deceleration such as in single-leg landing? In the absence of a comparison between model and experimental data from the single-leg landing trials, I am unconvinced that the model should be considered validated as the author states. How well do model kinematics match experimental kinematics? How well do model GRFs match subject GRFs? Did the author perform a sensitivity analysis to see which model parameters have the largest impact on the model results?	Were the foot - floor interface parameters the same for gait as in single-leg landing? Should they be? .The foot-floor interfaces was identical for the single-leg landing task and walking gait task. We are not sure why they should be different. Any difference would need to be reflected in the MSM, as well as data used for validation which most likely does not exist in the literature. And even if the gait model results were compared to literature values as in Table 1, how do we know the MSM will be valid in an impact situation with sudden deceleration such as in single-leg landing? . This is a very good question. The answer is: we do not know. However, the model used from this study is a Gait full body model, which is the most heavily worked on model in the Anybody repository with over 10 years of development. This model was extensively verified and validated by other research groups for gait. Outside of this to apply this model to our application we did various things to acquire confidence in the model such as sensitivity studies, comparison of outputs with Visual 3D and muscle modeling studies. Again, given this is an article style thesis this information was not added to the thesis given it was deemed unworthy of publication. The validation process used in this study is two-fold. First, we compared EMG measured with muscle activity from model. This is the classical approach and only approach used by many MSM studies. We have added time histories of measured versus predicted muscle activity, as well as the mean correlation coefficients of muscle activation measured versus predicted for 8 muscles. To acquire greater confidence, we went a step further with our model and endeavored to compare model predictions with *in vivo* data of knee joint reaction forces and moments during single-leg landings. Unfortunately such data does not exist. However, given *in vivo*

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		data on walking gait exist, we compared our model predictions with this. Given the efforts from above, we were given some confidence that our model is valid. In the absence of a comparison between model and experimental data from the single-leg landing trials, I am unconvinced that the model should be considered validated as the author states. How well do model kinematics match experimental kinematics? How well do model GRFs match subject GRFs? Did the author perform a sensitivity analysis to see which model parameters have the largest impact on the model results? Validation of models demands experimental data for confirmation. Such data are difficult to record and in many cases may never be obtained. As a paradox, this is actually the reason why models are developed in the first place. The validation of this work was to demonstrate that model produces reasonable estimates for muscle activation patterns during single leg landing, as well as joint reaction forces during walking. To date *in-vivo* experimental data on single-leg jump landing does not exist. It is not currently possible to fully validate MSMs since the data necessary to provide the validation would be too invasive (e.g., strain gauged tendons, ligament etc.). This study has attempted to validate the model using EMGs and comparisons with published *in vivo* studies having similar experimental conditions. This study used the best means currently available. We provided two separate comparisons for validation. The comparison of muscle activity from model with experiment is quite within what would expect from these sorts of model. For the most part this is the fullest extent to knowledge provided for model validation in the literature. Further, we are convinced that our results in table 1 would be better if the subjects from *in-vivo* studies and that from experiment were closer in weight. For the *in vivo* data subjects were at least 300N heavier that the average subject weight from our study.

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		The matching of model kinematics with experimental kinematics was within an error less than 0.5. This means the total difference between markers from experiment and markers from the model for all markers is less than 0.5 at the end of the optimization process. See sample output from objective function optimization (please see Attachment A). GRFs are used as inputs via the C3D file and unchanged in AnyBody. We performed many sensitivity studies – please see summary report (report 4), which includes studies on muscle recruitment criteria: Report 1; muscle model type (simple vs. hill): report 2; and, study to verify the large joint reaction forces and moment from developed AnyBody model: report 3.
12	· ***Omission of knee ligaments (including ACL) in MSM*** – In papers 1 and 2, the author champions the use of MSMs that will allow the estimation of internal forces acting on tissues within the body, important data that cannot be measured due to ethical considerations, and cannot be computed by standard rigid body inverse dynamics models. In paper 5 the author describes the use of a MSM, but I was very surprised to find that the MSM did NOT include the ACL, which of course is the main topic of the doctoral thesis. Why was the ACL (and the other 3 major knee ligaments) omitted from the MSM? Given the title and topic of the thesis, what was the rationale for leaving the ligaments out of the model? Surely the force (stress) and	The material properties, geometry, and constitutive law to model the four major ligaments of the knee joint is unknown or under research. The kinematics of the ACL during single-leg landing is also unknown in the scientific community. As well, ligament-bone and ligament-ligament interaction is unknown in the scientific community. The author is aware that 1D line elements can be used to model the ligaments, but this would be nothing more than a constraint (like a muscle) added to the joint to balance external forces. It seems that one dimensional assumption may be acceptable given that *in vivo* data to date on soft tissues such as the ACL are limited to force or displacement measurements. Almost all mathematical models developed to date for the knee use one-dimensional representation for the ligaments. This is mainly because of the belief that the primary function of the ligaments is to resist tensile forces. Although one dimensional representation can be used to predict ligament forces, they are unable to predict stress distributions.

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	strain that the ACL undergoes during the landings would be a valuable addition to the thesis?	
13	***.Data for males and females not reported separately in paper 5*** – In paper 5, the data and correlations in Table 3 are reported for all 6 subjects in aggregate, even though the purpose is to compare the male and female groups. The separate male and female data should also be reported, and indeed are the critical data needed to compare between male and female responses.	. Thanks for the feedback. All variables for males and females have been added in the thesis in two separate tables to facilitate comparison.
14	**.Contribution of the thesis to advancing knowledge:** This is difficult to judge until the data in papers 3, 4 and 5 are described in more detail.	More details have been added to the thesis as requested.
15	. **Research methodology:** The motion capture, force measurement and EMG data collection techniques used by the author are well established in the biomechanics community, as are the use of rigid body inverse dynamics models and musculoskeletal models. Due to lack of written detail, it is difficult to know whether the musculoskeletal models are really "subject-specific" as the author claims, and it is difficult to know how well these models represent the subject movements during the single-leg landing tasks. I do believe that the studies are under-powered due to low subject number.	. For each subject, musculoskeletal model was individualized so that model anthropometry matches subject anthropometry through a scaling law. This law is described in the paper. The inputs to facilitate scaling are subjects' body weights, heights and in some cases their segment lengths were adjusted. The later is done when the objective function residual from the kinematic modeling process yields high errors, which brings us to your second comment. To judge how well the kinematics from subjects matched model kinematics, an optimization routine was conducted. This process involved matching all markers measured by experiment to markers from the model. An error of below 0.5 or 0.1 is acceptable (see Attachment 1). In some cases, this is hard to achieve because of quality of data recorded in experiments.

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		. The study is not underpowered based on statistical ANOVA data reported. However, for the correlation studies we may have been able to obtain higher coefficient of determination and significance in areas where no significance was observed in our study.
16	.**Analysis of results and value of conclusions:** As described in the **General Comments** section above, the data in papers 3, 4 and 5 are not described in sufficient detail. This makes it impossible to fully understand the results of the experiments, and therefore the value of the conclusions. In my opinion, there are incorrect interpretations of at least some of the correlation data presented, leaving to some incorrect conclusions.	. This has been corrected throughout the thesis after many sit downs with Statistics professor from the school of human kinetics.
17	. As described in the **General Comments** above, I have major issues with the lack of detail in the material presented in papers 3, 4 and 5. I also think that chapter 7, currently titled "Discussion", would be better described by a title such as "Summary and Future Studies". As it stands now the chapter is not really an integrated Discussion of the thesis findings, but rather a serial summary of each of the 5 papers, followed by recommendations for future research. If it is to retain its current title, the chapter needs substantial revision to include integration of the important aspects of the different papers that is not present in the separate chapters themselves.	. Chapter 7 has been re-titled in the thesis as you suggested.
18	To accomplish this a problem is defined and formulated to determine the instance where many risk factors, many forces, and other extreme conditions happen simultaneously to	Thanks for the feedback. The answer is: we do not know, however, we can speculate that given the MDO paradigm can handle large-scale problems and take a global look at the problem, we may better be equipped to pinpoint the key factors contributing to injury and more importantly better understand the cause of the injury.

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	cause ACL failure. In the model how do we know if this will occur in any human?	
19	Kinematic data were low-pass filtered using a second-order bidirectional Butterworth filter at 6 Hz and analog data were filtered at 25 Hz. Why these cutoff frequencies?	. Kinematic data filtered at 6 Hz and force plate data at 25 Hz worked out well. We did tests to ensure these frequencies did not alter the raw data significantly, and retained a high percentage of the original signal content.
20	Page 99 on paper 3: Need to evaluate joint flexion, power and work over the entire time course of landing - not just one specific instant	. We are not sure how one will go about looking at knee flexion over the entire landing cycle to determine risk of ACL injury. Most studies assess kinematics, kinetics and energetics at a single point in time such as initial contact, peak VGRF, max knee flexion, etc. We specifically looked at one instant of time given it has been shown that the time of peak VGRF, for example, is the time at which peak ACL loads occur.
21	The results and discussion stemming from this study are only based on the theory of what is known about the relationship between ACL loads and GRFs. What does this mean.	.This means that peak ACL load occurs at the time of peak VGRF or some other peak value such as peak PGRF. For example, one in-vivo study that showed peak ACL load occurs at the same time as peak VGRF used only one male subject that performed a single leg hopping task. This is why all kinematics, kinetics and knee energetics were selected at time of peak VGRF. This approach is to assess risk of ACL injury and hinges on the validity.
22	Paper 4: Why knee abduction moment?	. The literature has shown that knee abduction moment may also predict the risk of ACL injury (Hewett et al. 2005; Markolf et al. 1995) .
23	Paper 5: How were subject specific muscle characteristics assessed.	. The MSM was made subject specific via scaling the anthropometry. The muscle characteristics were not made subject specific as this is not an easy task. Throughout this study, a simple muscle model using constant strength was used. The muscle strength of each subject was not measured during experiments. Note throughout the paper the word "subject specific" was removed and replaced with individualized.
24	Joint reaction or bone-on-bone?	.The joint reaction force will have a component of bone-on-bone contact

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		force. The reaction forces come out of the equilibrium equations and will have all components of the externally applied loads from gravity, the load from GRF, reaction forces from other joints, and forces from muscles. .Also we have modeled anatomical joints with simplistic idealized joints, for example, hinge joint for the knee, the reaction forces in this case represents what must be carried by the joint bone-on-bone contact and the soft tissue structures. In our model, we have a representation of the net loads in the joint and the direction of this load.
25	Vague how MDO does it work.	. We have added details to the thesis to explain this further. Keep in mind that the AI technique used in the MDO approach proposed is a black box as shown in Figure 2 of Paper 2. The AI technique functions to fuse existing ACL injury study approaches. We have added details on page 45-46 on how this can be done using OLE or DDE.
26	The AI technique is employed to orchestrate the fusion of the two quantitative study approaches in the MDO paradigm, as well as, to facilitate search and parameter identification. Commonly done in Biomechanics.	. Please provide a reference that shows where/how this is done in the field of biomechanics or more specifically, as per thesis topic, in the field of non-contact ACL injury biomechanics.
27	In this approach, the three qualitative study approaches are used for results validation. How? An AI technique also enables one to capture the wide variability in movement patterns to cause injury, and in tissue material properties, numerous design variables, numerous design constraints, many risk factors, and multiple objective functions. How? Vague	. Greater details have been added to pages 45-47 on how this can be done. The final figure provided in papers 1 and 2 also provide details on how to do this.
28	It is hypothesized that increasing height and distance of landing	. We believe it is a real hypothesis. For a non-living system such as an inanimate object, we would certainly agree with you, however the human

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	increases both the peak VGRFs and the peak PGRFs. Is this a real hypothesis? Doesn't Newton's law of acceleration predicts this?	body has muscles and the kinematics (landing technique) to dampen the loads from impact, even as vertical velocity and angular moment, increases. So, even when you increase height or distance, the ground reaction forces may not necessarily increase linearly as per Newtonian mechanics because the body aims to attenuate these forces. How the body does this is one of the aims of our study. Also this is a real hypothesis since we're dealing with a dynamic moving multisegment structure, in which each segment's acceleration and consequently motion is being produced by various muscles and also is being controlled quite case dependently. So, making a conclusion just based on Newton's 2nd law is practically underestimating our problem and does not seem to be a logical way to go.

Regarding you comments, we also could find no ISB standard for the knee joint. Further, many of the standards issued by ISB are not followed or more importantly enforced by scholarly publications, governments, university or industry.
ISEK standards for reporting EMG data is a good reference, thank you.

PhD THESIS REVIEW SHEET for Examiner C	
Document Title: Predicting risk factors of non-contact anterior cruciate ligament injuries during single-leg landing	
Revision: Final	
Author: Nicholas Ali	
Date Submitted:	
Related Docs/Reference: Four examiners reports, Original PhD Thesis and Revised PhD thesis	
Date Evaluated:	

No	Examiner's C Comments and location in Original PhD thesis	Authors' Comment
1	. While the sample size for the experiments is small, the results achieve statistical significance (for the population segment tested) and perhaps more importantly, partially illustrate the multifactorial analytical approach proposed by the candidate.	. The population of subjects studied were weight and height matched as much as possible. However, due to limitations of equipment and poor calibration of both the force plate and EMG system some of the subject data could not be used given force plate saturation and EMG system not working. Further, the test protocol had to be adjusted to remove the number and types of jumps performed by the subjects. Several subjects were added to papers 3 and 4 to increase statistical power. Tests show high powers were achieved.
2	The results are mostly properly described and analysed throughout the dissertation. Clearly, the most interesting material with regards to analysis of experimental data is contained in Papers IV and V. However, there is some	The results from papers 3, 4, and 5 were drawn from the same sample of subjects. A study by Louw and Grimmer titled "Biomechanical factors associated with the risk of knee injury when landing from a jump" (SAJSM Vol. 18, No 1, 2006) showed that only 8% of studies justified sample size used. Over 50 % of the studies included less than 20 subjects and the average age of subjects in all studies was 23 years. This study also

No	Examiner's C Comments and location in Original PhD thesis	Authors' Comment
	discontinuity in the results shown in both papers, although these results were assumedly obtained from the same set of experiments. This will deserve explanations during the oral defense and will likely justify revisions of the dissertation.	showed that males were more frequently studied than females. The authors using this as guidance and the feedback from committee members during the thesis proposal stage felt a sample size of 16 was sufficient for our objectives. Recall, initially the thesis proposal included only 6 subjects. No a prior power analysis was conducted. However, given force plate saturation and poor EMG data recorded some subjects data was removed from analysis.
3	. The organization and writing style of the material are acceptable, but would benefit from serious polishing and rewording/shortening of many unduly long and complex sentences. Many typos were also spotted. Many figures, graphs and tables are too small or too crowded a problem that needs to be addressed.	The figures and tables throughout the thesis were revised to make clearer. Further, many more time history plots, figures and tables were added based on recommendations from the external examiner.
4	Para 7: Paper IV essentially repeats paper III and goes further. Therefore, one should consider the deletion of Paper III for conciseness.	Paper 3's scope looks only at male subjects without a concern for gender effects. There is a high disparity in the ACL injury rate between genders. Why this disparity occurs is what paper 4 tries to understand. Paper 3 is focused only on height and distance effects on body kinematics and kinetics as well as knee energetics. Hence, the questions answered in paper 3 are very different from that in paper 4 although the experimental method employed is identical between the two papers. Given the dearth of information on knee energetics during single-leg landing from increasing heights and distance of landing, it was felt more effective report the results from our findings in separate papers.

PhD THESIS REVIEW SHEET for Examiner D	
Document Title: Predicting risk factors of non-contact anterior cruciate ligament injuries during single-leg landing	
Revision: Final	
Author: Nicholas Ali	
Date Submitted:	
Related Docs/Reference: Four examiners reports, Original PhD Thesis and Revised PhD thesis	
Date Evaluated:	

Examiner D

No	Examiner's D Comments and location in Original PhD thesis	Authors' Comment
1	. Revise paragraph format	It is unclear to us what change is required here.
2	. How much of the predictive nature of ACL injury is random and how much is predictable?	To date the answer to this question is unknown in the scientific community (please consult for example, Renstrom P. et al. BJSM, 2008, and Davis I.M. and Ireland M.L. 2001, Clin. Biomech.).
3	.The term "risk factors" is often used in a manner that leads the reader to question the appropriate use of this term. For example "To accomplish this a problem is defined and formulated to determine the instance where many risk factors, many forces, and other extreme conditions happen simultaneously to cause ACL failure." In my mind this includes environmental factors (ice, etc), footwear, medication, range of motion, balance, etc. More precise	"In my mind this includes environmental factors (ice, etc), footwear, medication, range of motion, balance, etc. More precise terms would be useful in many situations within the thesis." If this is what is in your mind, then the use of the term "risk factors" did not mislead you as all factors you have mentioned above are indeed risk factors. As highlighted in the thesis, there is much lack of agreement and confusion on risk factors implicated to cause injury, as well as how to categorize them. The risk factors may be categorized as biomechanical, environmental, anatomical and hormonal variables (Griffin et al. 2006; Renstrom et al.

No	Examiner's D Comments and location in Original PhD thesis	Authors' Comment
	terms would be useful in many situations within the thesis.	2008). Many studies have concluded that these risk factors are responsible for non-contact ACL injuries, but a large number of them have focused only on one or a few risk factors, thereby failing to capture all factors at once, as well as simultaneously considering the interactions of the different risk factors involved.
4	. The first two papers try to build a rationale for an ACL research methodology, but this method was not used in the thesis. Therefore, should these papers be included in this thesis?	The first two papers are review papers that endeavored to first highlight the barriers to better understanding the mechanisms and risk factors of non-contact ACL injury. From this review, the authors aimed to identify gaps in knowledge related the field of non-contact ACL injury. The authors went on to publish this work given many gaps in the literature identified can be used to steer future research direction. The authors tried to frame this review of the literature with the aim to bring some new insight and directions to this specific topic of research. Secondly these papers proposed a study methodology that may enable one to overcome the barriers to non-contact ACL injury research, hence its scientific contribution. To the authors' best knowledge, this information is absent from the literature. The details of this methodology is further elaborated upon, so that other researchers with larger budget, equipment, skill sets, and other resources can gain from this and perhaps employ it. The difference in the two papers' proposed study methodologies is that one is more refined than the other. This is a natural process of learning and development. Moreover, while many research groups have suggested that a multifactorial/multidisciplinary approach is required to address the challenges of non-contact ACL injury research, none of them has yet proposed a study methodology to do so. Thus, we think that these two papers are appreciable contributions to science. The authors offer the following email from a renowned researcher in the field of non-contact ACL injury research to the corresponding author on his views of Paper 1. Please note that Dr. Hashemi's work

No	Examiner's D Comments and location in Original PhD thesis	Authors' Comment
		was published after Paper 1 was published.
5	.Plantiflexion should be changed to plantarflexion throughout the document	Plantiflexion has been changed to plantar flexion. Plantarflexion is not in dictionaries.
6	.The word "gleaned" is used in the thesis. This can be changed, since the information is usually not "extracted from various sources" or "collected gradually and bit by bit"	We respect your point, but please note that various sources were indeed used, and hence word usage seems quite valid and logical.
7	.BW may be in N for paper 3 and Kg for paper 4 (Nm/BW*h). Please check and be consistent.	Please note that in both papers 3 and 4 forces were normalized to BW. So, we are consistent. In paper 4, the moments were normalized by the product of body mass and body height. We have stated BW* H, and this is incorrect as you have pointed out, so it has been corrected in all tables in paper 4. Thanks for your constructive comment.
8	.Do not replace commas with dashes. For example. "statistics -not presented- one can observe" should be "statistics, not presented, one can observe"	Thanks, change has been made throughout.
10	.Since arms motion was removed from the task, this should be considered with discussing the results	We think that this should have been suggested and discussed at the proposal stage, but not now. A point has been added to paper 3 through 5 to address this comment. In an effort to minimize the effect (variability due to swinging arms), the arms position during the single-leg landing task was standardized. The hands remained on the iliac crest throughout the landing task to remove the variability in landing mechanics due to swinging arms. Any reduction in the variability that can be obtained will result in greater statistical power and therefore reduce the probability of

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		committing a Type II decision error. The lack of standardization in the tasks (i.e. allowing swinging arms) may invalidate meaningful comparison. Subjects were not given any special instructions with regards to their landing mechanics to prevent experimenter bias. Further, the mass of the arms are small in comparison to the rest of the body, therefore their contribution to joint moments and forces are most likely negligible.
11	In paper 3, .Results must be clarified to indicate which results are linked to vertical, horizontal, or individual height analyses. .Results must be shown in tables for each height and distance condition (mean and SD)	. Change has been made to further clarify test for vertical height and test for horizontal distance in the thesis. See pages 95 and 96 please. . Tables with all means and all SD have been added to page 94 as well as other tables.
12	In paper 4, .The introduction talks mainly about the lack of literature but does not discuss the outcomes from the literature that does exist. This section needs to be rewritten to provide the reader with an overview of the existing literature on gender differences with single leg landing. This should cover both drop landing and jump to single leg lending since both topics are relevant. You can also discuss the	. Paper 4 clearly states that the study of single leg landing over increasing heights and distances that relate findings to risk of non-contact ACL injury is absent from the literature. Therefore this did not allow us to directly compare our findings with the literature. In the discussion, we highlight studies that look at a single height of two heights or compare single and double leg landings. . This comment should have been made at the thesis proposal stage. Please note that this thesis covers just single-leg landing, as was discussed and approved in the thesis proposal defense.

No	Examiner's D Comments and location in Original PhD thesis	Authors' Comment
	overall findings studies on just males and just females studies. .What post-hoc statistical tests were used to support statement of significance in the results (ex., Females had significantly less ankle plantiflexion angle than males)? .Post-hoc analysis is needed to explore the differences between conditions and groups .What range was used for the work outcomes? .Bring all mean and SD outcomes into one table (easier for the reader to examine outcomes).	Thank you for the feedback. At the thesis proposal stage a prior power analysis was not conducted. However, previous studies in literature such as the one provided to you at the thesis proposal defense (Louw Q and Grimmer K SAJSM 2006) that aimed to justify the sample size used for the thesis at the time (i.e. N=6) was provided. What was the outcome of this effort? Please be aware that the three papers in the thesis provides N, p and eta. Eta is a good measure of the degree to which the null hypothesis is false. Based on advice from supervisors, post-hoc studies were not conducted. However, at the thesis proposal stage similar studies on single-leg landing were reviewed to query subjects used and possible power. The total number of subjects selected initially was 6, and this was later changed to 16. . This is a good question. Work was calculated as the integral over the entire power curve from start to end of the task. The decision to use the entire motion was based on the idea that the negative power curve represents energy absorption by the extensor muscles (McNitt- Gray, 1993), thus it would allow a better representation of muscular energy absorption during the entire task. . This change has been made. All values consolidated into one table (Table 3 on page 129) except those influenced by gender of which figure 7a and 7b were added. . Tables fonts are larger. Necessary changes have been made throughout the thesis as requested.

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	Includes table 2, 4,6 .The font size is small. Tables could be revised if font size can be increased, but put these revised tables beneath each other in the manuscript. .It would be useful to have female, male, and overall mean and SD data presented, since the focus of the paper is on gender differences	.We think that these tables are not required as statistics revealed no differences between males and females except at ankle angles. For this, the means and SD were provided.
13	Paper 5: .See Kernozek, Torry, et al (2005) .Various aspects of the validation steps on pages 128-129 are unclear. .Specifics of the subjects, data, and activity used for Anybody input should be presented. .This section combines methods and results. Separating these may help to solve the confusion for the reader.	.Paper by Kernozek et al. is for a double-leg landing from a 60 cm height only while subject is hanging from a bar. We do believe no comparison is permissible with the findings of this paper. .Please let us know what is unclear. .Throughout the thesis all the sections has been revised to capture your requested changes. .Thanks for the feedback. Change has been made on page 130 to 131 to make this clear.

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14	.Page 24: "This work also appraises the methodological rigor"	.This change has been made on Page 24.
15	.Page 25: revise "has been somehow patchy"	.The authors believe that it is OK and so no change is required.
16	.FaunÃ is mispelled, check foreign language character sets.	.Thanks- change made FaunØ .
17	Page 27: ."side step cutting maneuvers, to name a few" ."view of ACL injury mechanisms"	. Both changes have been made on Page 27.
18	Page 29: "McConkey (McConkey, 1986) was the"	.This change has been made on Page 29.
19	.Page 30: "As well, muscle activity across the ankle controls the position of the foot at landing, which most likely influence the loading at the ankle" .As well, muscle activity across the ankle controls the foot position at landing, which most likely influences ankle loads.	. This change has been made on Page 30.
20	.Page 35: "Another, non contact method includes optical" .Rearrange paragraph to group contact and non-contact items	. This change has been made on Page 35.
21	.Page 37: "Computational modeling has become popular partly"	. This change has been made on Page 37.

No	Examiner's D Comments and location in Original PhD thesis	Authors' Comment
22	.Page 37: Remove "(see for instance"	. This change has been made on Page 37.
23	.Page 39: Reword "ACL injury research is a multidisciplinary field, since one need to consult with many disciplines in a single problem"	. This change has been made on Page 39.
24	.Page 25: "Nonetheless, the prevention of sport related noncontact ACL injuries today relies largely on the ability to screen at risk individuals and then modify through training the identified risk factor." .Screening for being at risk of ACL injury is not a common practice (i.e., foes not "rely largely upon) .Appropriate ACL at risk screening tools are not available	.Please let us know what you mean here, as it is unclear to us.
25	.Page 26: "are among the risk factors that can be modified through training" .Listed items are not risk factors	You are correct. Sorry for the mistake. Sentence should read: "Neuromuscular control strategies and muscle strength are among the risk factors that can be modified through training (Ageberg 2007; Bryant et al. 2008; Myer et al. 2007). Change has been made on Page 25-26
26	.Page 26: What is "hand searching", reading paper copies of journals? What journals were reviewed?	At the University of Toronto, most journals can be accessed hard copies at the library. Journals in the domain of bio, or bioengineering are catalogued this way and hence were viewed this way. Specific names of these journals are among those referenced.

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27	.Page 27: How did you determine that computing power was an obstacle for these studies? The choice to use slower computers does not mean that other computing options were not available.	Please read the sentence below from Page 27 which motivated this question and comment. "Fragmentation and discrepancies in the literature may be a reflection of the limitations and differences in current non-contact ACL injury study approaches which includes but not limited to, equipment used, computing power and software programs." Please let us know if we need to make further clarification.
28	.Page 27: What are the "the associated contributing risk factors"? What about the target activity and environment?	The associated risk factors can be broken down into four groups: environmental, biomechanical, neuromuscular, and hormonal (see Griffin et al. 2006). The activity is captured under kinematics and external loading, while the environment (e.g. playing surface) is a risk factor.
29	.Page 30: "that foot contact with the ground is an important risk factor in non-contact ACL injury" .Soccer players make foot contact with the ground with each step, typically without injury, therefore this risk factor statement should be reworded,	.Thanks for the feedback. Sentence has been amended on Page 31: By one study conducted using soccer players with varying cleat designs, it was also shown that cleats that produced higher torsional resistance with the ground is associated with higher risk of non-contact ACL injury (Lambson et al. 1996).
30	.Page 31: "ground reaction forces (GRFs) cannot be transmitted effectively through the **bones to the ground**" .GRF vector is from the ground to the foot	.Thanks for the feedback. This change has been made on Page 31: Another study found that when the foot was not flat, the ground reaction forces (GRFs) cannot be transmitted effectively through the bones from the ground without the actions of muscles (Anderson and Pandy 2003).
31	.Page 31: "the trunk and pelvis position will have coupled effects	This change has been made on Page 31 and 32:

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	on knee angles" .The knee angle may have effect on the pelvis and trunk …	Because the upper body contains over half of the total body mass, the trunk and pelvis position may likely have an effect on knee kinetics and resultant risk of ACL injury.
32	.Page 32: "The position of the leg at the time of non-contact ACL injury displays tibial rotation, apparent knee valgus, foot pronation, and a relatively extended knee and hip .You did not "display" this information in the paper. What situation is being described here? More detail is needed.	The argument being made in this section of the paper is that in order to study non-contact ACL mechanics one needs to include the ankle and hip articulations (please see title on paper 31 that states: **<u>Lack of studies that include ankle and hip articulation</u>**. This statement "The position of the leg at the time of non-contact ACL injury displays tibial rotation, apparent knee valgus, foot pronation, and a relatively extended knee and hip" is taken from findings by many researchers and written in this context to support the argument that ankle and hip inclusion in non-contact ACL injury research is indeed important. There is no specific situation being described as these kinematics can encompass varied injury mechanisms. Given this, we think that no change is required.
33	.Page 34: "These are termed contact methods and have the advantage of simultaneously including many risk factors," .How does an implanted transducer include risk factors? .All relevant muscles are typically not instrumented	You have taken the sentence out of context, and it seems that what was written was misinterpreted. The sentence read on its own will raise questions as you have here. For further clarity: .In-vivo testing using implantable transducers on human subjects, termed contact methods, has the ability to simultaneously include many risk factors given the human (which is difficult to simulate) is included in the study design while one accesses *in-vivo* data on tissues(s) of interest. By including the human in the study design one innately include muscle activation, joint forces, and applied forces. . Muscles do not need to be instrumented.

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	Which forces?	. Joint contact or externally applied forces. To date we do not know how to mathematically model knee joint contact forces with accuracy. Given this, we think that no change is required.
34	.Page 36: "The major advantage of in vitro testing is its utilization of biological tissue for testing" .In vitro can be defined as "In an artificial environment outside the living organism", so testing biological tissue need not be involved. .Testing in-vitro is a disadvantage over in-vivo, but necessary	. In vitro can be defined as "In an artificial environment outside the living organism", so testing biological tissue need not be involved. This is true as defined in the first sentence of this thesis section " . As per thesis "*In vitro* testing is conducted outside of the body typically with human subjects or post mortem human subjects (PMHS)/ cadavers. So, yes as per statement above we agree biological tissues need not be involved. . Point taken. Given this no change is required.
35	.Page 36: "In vitro testing also has the capability to simulate knee kinematics and muscle loads." .You could also use in-vivo data to drive a simulation	. I have added a sentence on Page 34 to incorporate this point for completeness- thanks for your comment.
36	.Page 36: "Other challenges with in vitro studies using cadavers are the inability to simulate realistic muscle activation and the difficulty in obtaining repeatable results" .This is the same thought as the previous sentence. .Repeatability is difficult in any biomechanical data collection with people	We have made the changes on Page 36 for further clarity: . Other challenges with *in vitro* studies using cadavers are the inability to simulate realistic and high muscle forces and the difficulty in obtaining repeatable results. .Agreed but it is even more so a challenge for in vitro studies using cadavers primarily due to the absence of muscles. Hence, without muscles cannot have repeatable kinematics (Blankvoort 1988, Naval MSc. Thesis).

No	Examiner's D Comments and location in Original PhD thesis	Authors' Comment
37	.Page 36: "Despite its shortcomings, in vitro studies have the capability to provide much freedom to investigate function and behavior of the ACL." .What is meant by "freedom" in this case?	.Ethical policies governing testing with humans limit the use of *in vivo* testing on humans. This limitation does not apply to *in vitro* testing.
38	.Page 36: "From this standpoint, it can be argued that gait analysis is the only way available today to determine the kinematics and kinetics during activity to cause non-contact ACL injury." .Kinematics and kinetics of what? Kinematics and kinetics of muscle-bone-ligament are typically poorly defined by gait analysis. .Can whole body kinematics and kinetics (joint angles, net joint moments, etc.) truly show the cause or just a possible body position and external loading scenario for injury? Only if you actually measure an injury?	This sentence has been revised on Page 36 to the following: From this standpoint, it can be argued that *in-vitro* studies is perhaps the only way available today or the best starting point to determine the kinematics and kinetics during activity to cause non-contact ACL injury. .This exact comment was raised and addressed by the student at the thesis proposal stage. It is not clear that what was the outcome of this effort by the student and why this question is being asked again at this stage?- please clarify.
39	.Page 37: "A computational model of the knee joint is a graphical representation of the joint anatomy" .A computational model does not have to be graphically represented to be used (i.e., a computational model is not a graphical	. Nowhere in the quote do the authors speak of "use". However there is some merit in adding the word "mathematical model" to the sentence. Change made on Page 37 to: A computational model of the knee joint is a mathematical model that can graphically represent the joint anatomy and motion.

No	Examiner's D Comments and location in Original PhD thesis	Authors' Comment
	representation, but can be represented graphically) ."A computational model is a mathematical model in computational science that requires extensive computational resources to study the behavior of a complex system by computer simulation"	
40	.Page 38: "The main advantage of musculoskeletal RB modeling is that it enables us to determine the forces in the muscles during activities implicated to cause non-contact ACL injuries" .Change "determine" to "estimate"	. Change has been made on Page 38.
41	.Page 39: "This may exacerbate itself to much uncertainty in theories used for teaching clinical biomechanics" .What do you mean by "This may exacerbate itself to much uncertainty"? Lack of consensus on theories? How does a lack of consensus make things worse when teaching? The instructor would present both schools of thought.	The authors appreciate this respected examiner's viewpoint and see no serious requirement for amendments. Given this no change was made.
42	.Page 40: "reductionist approach by focusing on a single factor or few factors due to small sample size." .Small sample sizes are not the reason for using methods that have a small number of variables.	. The sentence has been reworded on Page 40 to: Finally, the low annual incident rate for ACL injury in the general population of 1 per 3000 people (Malinzak et al. 2001) -and even smaller in the athletic population- has posed challenges for researchers aiming at

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	.If over 250,000 ACL injures are reported each year in the USA, a reasonable sample size for a study can be achieved .The cost of a large study may be the real problem	pinpointing factors contributing to risk of ACL injury since employing a large population of subjects in study design can be costly.
43	.Page 40-41: Various items in this proposed methodology are difficult to achieve: .That "close to injury joint kinematics" were achieved .Accurate "tibial displacement relative to femur" .Accurate "muscle tendon moment arms and lengths as well as muscle forces" for people that deviate from the model .Since the relative tissue/bone values that are modified by the AI could be wrong but create the desired output, having equivalent net joint moments, etc. does not necessarily validate the model ... it just shows that equivalent net joint outcomes could be generated.	There is immense work, cost, and resources from a large research group with varied skill sets to undertake this methodology. .Like the work of this thesis, you need to focus on a motion to create a framework for which you intend to study. If single-leg landing is your scope, then experiments of this nature should first be conducted to obtain physiological motions and possible close to injury situations. The experiments conducted in the lab for this thesis are done to assess the effect of heights, distances, and gender on body kinematics and kinetics during single leg landings. This motion can then be applied to drive a model. Once this model can be validate via some order of magnitude exercise, then it can be applied in a virtual environment by perturbing it, or using an optimization tool to help you better study injury. It can be argued that the only way to study injury is via a virtual environment using physiological inputs as a starting point and an optimization tool to search and find the injury situations. . Obtaining accurate tibial displacement relative to femur was never a claim made in this thesis. No change required. . Obtaining accurate muscle tendon moment arms and lengths, as well as muscle forces were never a claim made in this thesis. The authors do believe that in the future MSM tools will enable one to customized muscle moment arms to subjects body, but from a cost benefit accuracy tradeoff point of view the authors feel this can be a useless exercise. The methodology as proposed does not use anatomy as a design variable.
44	.Page 43: ."Nonetheless, this approach allows	.We do understand your concern, but in the biomechanics community

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	for virtual experimentation which has significant implication for cost reduction through reduced equipment needs, number of subjects required for testing, and also time for testing." .Virtual experimentation would reduce costs if a "perfect" model was built that answered all questions. Since this is not the case, costs are still present to verify if modelled outcomes apply well in the real world.	validating whether a computational model outcome applies well to the real world is not a limitation of this thesis, but a limitation of science. Given the empirical tradition of the biomechanics community, one may argue that computational modeling software were perhaps slow to develop compared to that in the engineering community which undertake numerous virtual experimentation as a cost saving initiative. Further, we think a really good question is to find a study in non-contact ACL research that employs an MDO paradigm. The method is new to the field of biomechanics and if applied to the field as it is envisioned by Dr. Lloyd, Thomas Buchanan, Quatman, Marco Viceconti, Herbert Hatze etc. can yield great benefits. Herbert Hatze at the Geoffrey Dyson Memorial Lecture said that it will become obvious that a large class of problems confronting the sports biomechanists can be ultimately identified as belonging to the field of optimization.
	."In addition, one of the central aims of this proposed approach is to provide an enabling tool to better capture the many variables, constraints, unknowns, uncertainty, and variability entailed in the complex problem of predicting injury mechanisms and identifying risk factors of non-contact ACL injury." .How do you capture unknowns and uncertainty? .It is unclear how the tools helps with this sentence .What do you mean by "capture the interaction" ."This approach should also aim to provide information that can	The application of MDO study paradigm is novel to the biomechanics field. MDO is a system science or system modeling approach to solving complex problems. The researchers mentioned above are among few who are critical to the conventional approaches used in the biomechanics field.

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	connect the cause and effect relationships between ACL loading, injury mechanisms, and risk factors of noncontact ACL injury." .What information would you be providing, for example	
45	.Page 44: The first paragraphs is confusing. After rereading this many times, the author initially states that the model should provide various outcome measures but then states that the kinematic information to create this model is not available so this cannot be achieved? ."One approach to resolve this challenge may be to conduct parametric and sensitivity studies" .Studies of what parameters? .An unreasonable number of studies would be required to eliminate what does not produce an injury, with the objective of only leaving conditions that cause an injury. Therefore, this is not a viable approach	. Quite the contrary. The exact kinematics at the time of ACL injury for side-step cutting or single-leg landing is unknown. It is for this reason that one starts with close to injury situations in the laboratory using a computational model. Now assuming you have a validated computational model, how do you begin determining the mechanisms and risk factors for ACL injury? The few attempts to do this result in many difficulties given there are likely too many parameters at play during non-contact ACL injury event. To resolve this, one can do sensitivity studies which have its pitfalls as highlighted in the thesis. . . Sensitivity studies on variables one feels may or may not be a contributor to the risk of non-contact ACL injury. If there is no effect, then remove it from the problem scope. ."An unreasonable number of studies would be required to eliminate what does not produce an injury, with the objective of only leaving conditions that cause an injury. Therefore, this is not a viable approach." You may very well be right, but this is yet to proven. Sensitivity and parametric studies are a common reductionist approach to solve problems.
46	.Page 46: How can AI be used to "define a problem" .It is unclear how data from different people, different,	. This is a good question, thank you. Within the context of this thesis one can set up the objective function such as to enable the computational model to find the variables that causes the stress at the ACL to exceed yield stress within certain set

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	injuries, and different conditions can be fused to generate useful information, using the proposed input data.	variables and constraints. One will also impose physiological constraints. The objective function and constraints to capture the numerous factors involved. . Please highlight where on Page 46 such a claim is made.
47	.The author states an approach but has not provided a sufficient rationale as to how this can be implemented in practice.	. This is good point. We assume that you understand then "why the proposed approach should be implemented." Many research groups investigating non-contact ACL injury recognize that the problem is multifactorial/multidisciplinary. However, many researcher groups never proposed a way to handle such a problem. The authors of the Paper 1 and Paper 2 has endeavored to fill this gap. It is for this reason that both Paper 1 and Paper 2 are appreciable contributions to science, we believe. Further, determining how to implement this approach is beyond the resources and skill sets afforded to this thesis.
48	.Page 46: "A case was not proven that "the narrow focus of some studies and the dearth of standards and specifications in the field of biomechanics appear to have the effect of limiting progress". Past study methods and standards do not limit how a research can make an advance in the ACL field. Methodological and ethical issues are more likely the limitation.	. The goal of a review paper is not to prove anything but to present what is known about the area of research and further synthesize all the unconnected topics into an integrated "state of the science" review. We will be very happy if this respected examiner can provide a specification or standard used globally by all researchers that can find direct application to non-contact ACL injury research. The paper has been published so further discussion of its merits are irrelevant.
49	.Page 47: Creators of ACL injury prevention programmes know how their system works. There is likely not one key element, so looking for such an element may not be warranted. The holistic approaches	. What system are you referring to?- it is not clear to us. We cannot prevent or design training regimes for something we do not understand. As an example, we would be keen on seeing the body of literature that shows agreement, for example on "flexibility" "or perhaps "increasing strengthen" or any of the other variables you have mentioned, as a contributing factor to non-contact ACL injury. The

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	of avoiding vulnerable positions, increasing flexibility, increasing strength, including plyometric exercises in training, and increasing proprioception should be considered.	question then one is compelled to ask is, why is this the case? Some of the answers are in Paper 1 and Paper 11. The proposed study paradigm can capture the factors that this respected examiner has mentioned and many others in a single problem definition. The paper has been published so further discussion of its merits are irrelevant.
50	.Page 58: Revise page numbers in paper reference	This change has been made on Page 58.
51	.Page 70: "compare rigid and deformable contact scenarios"	This change has been made on Page 70.
52	.Page 71: "multivariate function that" ."The Levenberg-Marquardt algorithm can be thought of as a combination of steepest decent and Gauss-Newton methods." ."This method was modified by Fletcher (Fletcher, 1971) to tailor the amount of dampening used at each iteration so as to" ."Powell (Powell, 1978) to solve an over constrained system of equations via least squares optimization" ."The authors used an AI technique, simulated annealing, to determine" ."Monte Carlo simulations were"	This change has been made on Page 71. This change has been made on Page 71. This change has been made on Page 71. This change has been made on Page 71. This change has been made on Page 72. This change has been made on Page 72.
53	.Page 72: "Mclean et al. (Scott et al., 2004)" .Check reference and spelling of McLean. If reference from Scott's paper, put year of the McLean work.	. Spelling of McLean is correct. However the references have been revised to use Scott's last name. Change made throughout the thesis- thanks for your comment.

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54	.Page 75: "determine if the model can be considered valid."	. This change has been made on Page 75.
55	.Page 61: What is "combined loading" ."Non-contact ACL injury is also a whole body phenomenon that is best analyzed by simultaneously addressing multiple risk factors of which neuromuscular control, joint kinematics and geometry, as well as, external forces that may be the most important." .Are the external forces the most important or other items in the sentence? How are you proving which is the most important (include reference, ...)? .Video analyses are not necessarily qualitative. They may measure frequencies of injury situations, etc.	. Thanks for the feedback. The paper has already been published.
56	.Page 69: What is meant by "Intra subject variabilities may stem from technician performing experiments"?	. Variabilities during experiment within a subject can stem from investigator managing the experiment. Hence, the way instructions are communicated to subjects, equipment setup and calibration etc. from one day to the next may be different and lead to variabilities when testing the same subject.
57	Page 70: ."A later study by Blankvoort et al. (Blankevoort and Huiskes, 1996) used the same mathematical model" .Which one, Blankvoort et al.,	. This has been amended for better clarity. The answer is Blackvoort et al.'s 1991 model. Change made on Page 70. "This model was validated in a later study by Blankvoort *et al.* (Blankevoort and Huiskes

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	1991, Wismans et al., 1980? ."for usage in the model" .Which model? ."Blankvoort research group employed an optimization scheme to estimate the initial strains since no experimental data was available" .You said that the previous model was used in the last sentence? .I do not understand "experiments via the variation of the reference strains in the ligament". Are these other experiments on people?	1996) whereby the effects of the initial strain of ligaments were included." . See change made on Page 70. . See the change made on Page 70 that clarifies this. . Blankvoort (1991) advanced the knee model developed by Wismans (1980) by including deformable contact at the tibiofemoral surface and the effect of ligaments wrapping around bones. The earlier model of Blankvoort (1991) showed that modeling the articular cartilage as a deformable body by adjusting the stiffness properties had little effect on model characteristics. Given this, Blankvoort later conducted a study (Blankvoort 1996) where only the initial strain of ligaments were included. Blankvoort used an optimization scheme to estimate the initial strains since no experimental data was available. Optimization was based on minimization of the difference in kinematic between the knee model and that experimentally obtained by variation of the reference strains in the line element. The ligaments were modeled as 1-D elements. Comparison of knee model's passive motion with experiment was done with data from the literature obtained from earlier studies by Blankvoort's research group (1991) using knee specimens.
58	.Page 72: .Monte Carlo methods are algorithms that randomly generate and retain the best solutions before going to the next search iteration." .This does not seem to be the case for Scott et al, 2008: "The Monte Carlo approach adopted within the current study necessarily considered each perturbed input parameter as independent from the next. In other words, for that N-	. As per the thesis that referenced McLean's 2008 paper, Monte Carlo simulations were also performed by the authors to determine the effects of variability in neuromuscular control on peak anterior drawer force, valgus moment, and internal rotation moment. In general, "Monte Carlo methods are algorithms that randomly generate and retain the best solutions before going to the next search iteration." It should be noted please that this is a weakness of Monte Carlo methods in comparison to AI approaches that can simultaneously handle numerous solutions in each iteration. . Perhaps this sentence should be reworded as

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	dimensional space, we necessarily sampled input conditions from all corners of the hypercube. Adopting such an approach meant that some of the combined perturbed conditions would be highly unlikely in vivo, with performance of a successful sidestep being virtually impossible in these instances."	"With regards to application to Biomechanics, Monte Carlo methods are used primarily to evaluate the probability of random outcomes of human movement." Please let us know if this is OK.
	."Monte Carlo method is used primarily in this application to evaluate the probability of random outcomes of human movement." .This does not seem to be the case for Scott et al., 2008	.This sentence is not supported by the reference. This sentence is our own and no reference is required. Thus, no change has been made.
	."Monte Carlo simulation is an attractive tool since it allows researchers to study and predict risk of sustaining an injury before injury occurs." .This sentence is not supported by the reference	. "does not seem" is quite vague. Please clarify for us.
	."However, simulated annealing is simply mentioned by the authors but the way the method is employed to answer the author's research question is not clear .Scott provides both the equation	. This sentence was not used in relation to McLean et al.'s (2008) work.

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	and reference for the simulated annealing approach	. Yes, the way the method is employed is not clear to us even with this equation and reference. To state just the objective function is not enough. If the problem is clear to you, can you please provide us the answer to the following question: What are the constraints or constraint method use in this study?
59	.Page 73: "whether sagittal plane knee loading during sidestep cutting could in isolation injure the ACL" .How is the injury isolated if the person is sidestep cutting and a load is applied?	. This statement is aligned with the objective of the study by Mclean et al. 2004. As per thesis the sentence reads: "McLean *et al.* (McLean et al. 2004) also applied the identical optimization methods to examine whether sagittal plane knee loading during side step cutting could in isolation injure the ACL." In the study by McLean et al. 2004, a model was used to predict the effect of perturbations in neuromuscular control (NMC) on resultant knee movement and loading. The effects of random variations in NMC during the stance phase of sidestep cutting on 3D knee loading was determined. What the author did is as follows: they investigated the effect of ONLY sagittal plane loading mechanism, comprising of quadriceps and hamstring forces, flexion angle, and external anterior-posterior joint loads (values looked at in isolation using the model) on potential to injure the ACL between genders.
60	.Page 74: "The AI technique is employed to orchestrate the fusion of the two quantitative study approaches in the MDO paradigm," .What are the MDO study approaches?	Please see Figure 2 on Page 76 where the MDO approach is presented.

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61	.Page 74; It is unclear how clinical studies, interviews with athletes, video analyses will be used for validation	. As you have correctly pointed out earlier, it is possible that an AI technique can result in poor solutions. To help guide the search and optimization routine the problem must have some constraints. This is a mandatory process in ALL optimization problems. The process of constraining the problem will enable us to determine physiological results. The constraints can be determined from qualitative studies such as those reported in the literature from clinical studies, video analysis, etc. As an example, from video analysis, we know that typically ACL injury occurs during single leg landing when knee is in extended position and upper body away from the knee. Given AI can handle large ranges for any given variable, we can use this information to limit the range of knee flexion and trunk flexions for example in our problem definition.
62	.Page 74: "An AI technique also enables one to capture the wide variability in movement patterns ..." .AI can also generate a wide variety of incorrect results	. Please see answer to question # 60 that can help us understand how to prevent this. The following references were added to the text to support your comments: Such a study approach may be a much more robust and comprehensive methodology to better predict non-contact ACL injuries (Lloyd et al. 2008; Quatman et al. 2009). An AI technique is preferred over OR techniques for non-contact ACL injury studies since they do not require a mathematical function, are more robust in dealing with both qualitative and quantitative variables, enables a system-based type of approach to solving complex problems (Carla 2000), and above all, they share an enhanced ability to handle many design variables and constraints over a large multimodal search space (Brown and White 1990; Holsapple et al. 1994).
63	.Page 75: "The external forces, muscle activation, and muscle forces at this specific lower extremity kinematic should ..."	. Lower extremity kinematics refers to the 3D kinematics of the ankle, knee and hip.

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	.What do you mean by a "lower extremity kinematic"?	
64	.Page 77: "It was shown that present challenges in non-contact ACL injury studies stem partly from the inability of existing study approaches to simultaneously capture numerous factors and parameters which are at play during ACL injury." .This was proposed, now shown (i.e., shown is usually associated with evidence, such as evidence that more factors and parameters improve clinical practice). Since error may increase with more parameters, we cannot assume that the final outcomes will be better for a particular method. .Based on this paper, the thesis should combine "biomechanical, environmental, anatomical and hormonal variables". The thesis does not include hormonal or environmental factors ."AI technique is better suited to address present challenges" .Better that OR?	. This paper did expose some of the challenges with existing ACL injury study approaches with the aim of first determining the reasons for these challenges, but more importantly how one can go about overcoming these challenge. Given this, the use of the word shown seems appropriate. Since error may increase with more parameters, we cannot assume that the final outcomes will be better for a particular method. .This is not an issue of errors occurring due to many variables or rounding errors in various stages of analysis: What the proposed MDO approach offers is a scientific method to address the challenges in non-contact ACL injury research. What the approach brings to the forefront is the ability to tie together many disjointed disciplines or departments in single environment so that systems approach to problem solving can occur. This can be done via AI which is a scientific contribution. The five existing ACL injury study approach all have their strengths and weaknesses. Part of the authors argument is that science still does not understand how and why ACL injuries occurs given each existing study approach when used on its own can only address part of the problem and negates many aspects in the problem definition. AI can overcome this challenge. We may all agree that only a multifactorial/ multidisciplinary approach that fuses together these study approaches or is able to capture the variables in the 5 existing study approaches may overcome this obstacle. Now how does one go about this?. The answer lies in the use of an optimization approach. The authors have provided reasons why AI is preferred and how it can be used. We have added more details to the paper to show how this can be

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		done. The paper has already been published. . This thesis is an "article style" thesis. Each paper with its own objectives, methods, and results. The second published paper does highlight the domain of the known risk factors and how they are ALL captured in the MDO study paradigm. . Yes better suited than OR. Change made on Page 78.
65	.Page 87: ."the relationship among sagittal plane body kinematics, knee power, knee work and peak GRFs." ."single-leg landings from platform heights of 20, 40, and 60 cm" ."Subjects also performed single-leg landings from a 40 cm height platform placed 30, 50 and 70 cm from the rear edge of a force plate" .Define first instance of VGRF, PGRF	. Change made Page 87. . Change made on Page 87. . Change made on Page 87. . Change made on Page 87.
66	.Page 88: "knee joint, two key factors"	. Change made on Page 88.
67	.Page 90 "that hip external rotation strength had"	. Change made on Page 90.
68	.Page 91: "Motion capture system (Vicon MX, Oxford Metrics, UK) consisting" to A seven camera motion capture system (Vicon MX, Oxford Metrics, UK) was used to collect …"	. Change made on Page 91-92.

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69	.Page 92: "were instructed to stand on a variable height landing platform (20, 40, and 60 cm)" ."All kinematic data and analog data were low-pass filtered using a second-order bidirectional Butterworth filter at 6 Hz and 20 Hz, respectively." .This sentence could be rewritten so that the reader does not have to reread the sentence to understand, due to the use of respectively. For example, "Kinematic data were filtered using a second-order bidirectional Butterworth filter at 6Hz and analog data were filtered at 20 Hz.	. Change made on Page 92. . Change has been made on Page 92.
70	.Page 93: "correlations were also used to" ."finding of this study (Fig. 2) was that the horizontal" .No highlights/shading were show in Fig. 2.	. No change required as two sets of PPMC analysis were conducted. . I appreciate your suggestion. Change made on Page 93.
71	.Page 97: "Our results corroborate these findings showing that by increasing ankle plantar flexion, there"	. Change made on Page 97.
72	.Page 98: perhaps too short to allow the muscles surrounding the ankle and knee to respond."	. Change made on Page 98.

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73	.Page 99: ."Further, at an increasing landing height, hip and trunk flexion may be more appropriate for attenuating GRFs" both eccentric ."knee power and eccentric knee work were positively and significantly correlated to both peak VGRF"	. Change made on Page 99. . Change made on Page 99.
74	.Page 87: "more appropriate for jump landings" .You have shown that hip-trunk or ankle-knee strategies are used by the subjects, but not that these are the most appropriate.	. Our results suggest that at increasing vertical heights, hip-trunk strategy seem to be used by the subjects while for increasing distance, an ankle knee strategy is used. We have revised this statement to your recommendations. Change made on page 88.
75	.Page 90: "Although the above-mentioned studies reported valuable findings, they lack data concerning sagittal plane kinematics and kinetics of the ankle, knee, hip, and trunk at increased height and distance of landing" .Combining the studies covers a range of heights and they do report flexion/extension biomechanics	.The identical comment was raised at the thesis proposal in which several papers were presented as being identical (see Attachment A). In addition, this comment was raised and addressed by the student at the thesis proposal stage. What was the outcome of this effort by the student and why is this question being asked again at this stage? Further no single-leg landing studies exist that look at increasing vertical height and horizontal distance. Secondly you cannot combine studies due to tremendous heterogeneity between studies as raised in the review of the literature paper we published as well as discussion from each paper's introduction. Please see Attachment A.
76	.Page 91: .Describe the identical shoes (brand, etc.) .Define the "customized marker protocol"	. The shoe used is ASICS running shoes, model BY004, ASICS America Corporation, Irvine, CA). Change made on Page 91 and this detailed added to all papers. . The Vicon Plug-in Gait marker set was customized to include

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		additional markers at the hip and medial aspects of the elbow, knee and ankle, as well as additional foot markers. Different marker locations were also used at the proximal ends of the pelvis and around the head. Change made on Pages 91 and 92. Furthermore, this change has been made on all papers.
77	.Page 93: .If you are referring to the maximum VGRF, use this term instead of peak. A curve can have many peaks but only one maximum. .0.8 s before VGRF is a long time, is this correct? The entire stance phase in walking can be shorter that this time. A quick check of the literature shows 50-70 ms for time from foot strike to maximum VGRF in a jump landing and the entire event is over within 0.5 s. .Using time as the basis for work calculations can create error, as opposed to event-based criteria, since timing between individuals varies	The first comment has merit but it is not valid. For a single-leg jump landing, there is only one clear distinguishable peak. See Figure 1a in Paper 4 for a good example. . Yes, 0.8s is correct for time take prior to maximum VGRF. The reason for this is first that the subject stands on both legs, transfers the weight over to the dominant leg, and then jumps. This is what takes time. "A quick check of the literature shows 50-70 ms for time from foot strike to maximum VGRF in a jump landing and the entire event is over within 0.5 s." Yes, this is perhaps true, but for what type of task? For a vertical drop jump, maybe. So step one, peak VGRF is a clear and unambiguous event to capture. The end point being plus some time or percentage is very reasonable, because once balance has been established you would not expect large VGRF and visual inspection will verify the rationale for terminating the analysis. This leaves only the starting point, and this can be a bit vague. -0.7 second or -% from peak VGRF is a great way to standardize, because it removes issues of take off mechanics and simply states I'm only interested in what happens after this point, but prior to landing. I think this rationale stands up because the metric of interest is VGRF and the variation in the time in the air is essentially not important.

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		"Using time as the basis for work calculations can create error, as opposed to event-based criteria, since timing between individuals varies." Thanks for the comment. Events were created and used for all studies.
78	Page 93: .Did you use 2D sagittal plane kinematics or 3D flexion-extension for the analysis? I is unclear why you would take 3D data and deconstruct this to 2D sagittal plane analysis, especially since the leg typically rotates out of the sagittal plane during landings. .Correlations <0.7 are not high. Do you mean relatively higher that some other analysis? Typically, 0.2 to 0.4 Weak, low correlation (not very significant); 0.4 to 0.7 Moderate correlation; 0.7 to 0.9 Strong, high correlation; 0.9 to 1.0 Very strong ."knee work as determined at the time of peak VGRF" .Work is typically over a range and not at a single value. How was this calculated?	. Joint 3D kinematics were used. No deconstruction was used. Only data from a single plane used given single leg landing is sagittal plane dominant. This is a good point. The errors in camera calibration, as well as, the skin movement artifacts can be higher in magnitude that the amount of joint movement measured in some planes for the task. This is the case for transverse plane movement data such as tibial rotation, where it has been shown in the literature that skin artifacts for this measurement are larger than the measurement itself. . For clarity please note that this contradicts your comment made later in this review, where you speak to abduction moment. . It is unclear to us how you established that correlation < 0.7 is not high. Please provide reference on the "typical values" suggested. The r=0.698 is taught to be high in this case given the low number of subjects used. .This comment is repeated. This was a mistake in wording. Work was determined over a range, but wording has been to change to reflect this. Power is the product of joint moment and joint angular velocity. This yields a curve when integrated yields work done on a joint. Using events one can mark the location of peak VGRF and integrate from start of task and end at time of peak VGRF. This change has been made throughout the thesis.

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	."The means and standard deviations of the sagittal plane body kinematics, knee power, and knee work" .Is this the mean and SD across all subjects? Please specify for text and figure captions. ."There were no significant relationships between peak VGRF and ankle or knee flexion; however, our results indicated significant correlations between both hip and trunk flexion and peak VGRF." .For which tests (vertical or horizontal)?	. Yes, it is the mean and SD for all subjects. Change has been made on page 92-95. . Greater details have been added to the thesis to better clarify your concern. The necessary change has been made on Page 93.
79	.Pages 94, 95: .In methods you indicated 6 different tests, landing from 20, 40, 60 cm and landing from 30, 50, 70 cm; however, the tables on page 94 only provide one set of means. Is this the overall mean for all trials? .Mean and SD for all subjects need to be shown for each test condition .In Figures and tables, state which test conditions are being displayed in the caption. All conditions have VGRF and PGRF values so you need to specify what the reader is seeing. .Without the data for each trial, I cannot tell from the scatter plots	. Yes, it is the overall means and SD for all trials. The sentence has been amended on Page 93. .The tables of all means and SD have been added to you here as well as throughout the thesis. . The change has been made to the tables. No change required on the figures given the type of test should be obvious from *x* axis label. Thank you. Tables have been added to the thesis. There are six data points, one for each subject at each vertical height and distance (see

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	how each person varies between conditions. .Correlation matrix is stated but only one column of data is displayed.	Fig 1 and Fig 2). This paper has a set objective, thus the variation in other variables for each condition across subjects was not presented. . This is a good point. The word matrix is deceiving. Change has been made throughout the thesis.
80	.Page 96: ."Results of this study showed that ankle and knee flexion to be moderately and significantly correlated with peak PGRF" .0.395 is a weak correlation ."Interestingly, no significant correlation between peak PGRF and hip flexion or trunk flexion was found." .The weak correlations are more interesting than the significance, significance only states that the results is likely not by chance. In these cases, the correlations are low but this result may just be by chance. ."It was also observed that both the eccentric knee power and eccentric knee work demonstrated a moderate to high negative correlation with both the peak VGRF (r=0.493, p=0.037 and r=0.63, p=0.005, respectively) and the peak PGRF (r=0.63, p=0.005 and r=0.475, p=0.105, respectively)." .0.63 is moderate, not high	. 0.395 is a weak correlation depending on which guidelines you follow and on what you are measuring. The following guidelines was used: 0.1 to 0.3 weak 0.3 to 0.5 moderate 0.5 to 1 strong . The following guidelines was used: 0.1 to 0.3 weak 0.3 to 0.5 moderate 0.5 to 1 strong Hence the use of the term "high"

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	.You stated negative correlations but the r values are positive .It will be easier for the reader to understand this statement if they can see the results for each condition in a table ."Results of this study (see Fig. 1 and Fig. 2) support the findings of other studies that investigated a completely different event but demonstrated a significant correlation between peak GRF and risk of knee injury" .This study does not make a link between peak GRF and knee injury risk, and figure 1 and 2 only show a trend between greater GRF for higher and longer jumping distances, as previously known. ."Our results showed that at increasing vertical heights, knee flexion was not correlated to peak VGRF and therefore may have little potential for reducing the risk of non-contact ACL injuries during single-leg landings." .This statement is not supported. Even though the six subject's used a different strategy for dealing with landing forces, this does not mean than bending the knee cannot be used as a strategy. ."This does not corroborate the	. This is a mistake. The *r* values should be negative. Change has been made throughout. . Repeated comment. This is a duplication of comment made earlier with regards to presenting means and standard deviation for all subjects at each trial. We have provided throughout the thesis the table and figures you requested. . If it is already known that greater vertical heights and greater horizontal distances leads to higher GRFs, then please provide us the reference(s) that show this. Remember we are dealing with a multisegment structure. Further, this is only one aspect of this study. Once the effects of height, distance and gender are established, what is happening in terms of body kinematics, muscle and joint reaction forces, knee energetics as height, distance and gender change was also investigated. Further, what is the effect of these changes on risk of ACL injury? Given the study protocol was presented to you at thesis proposal stage, we are wondering why was this not raised at that stage? .In this study, peak VGRF and peak PGRF are used as risk predictor variables. Given increasing heights leads to increase GRFs, then there is increased risk of non-contact ACL injuries at higher heights. It has been shown in other studies, as can be found in the thesis, that peak ACL loading occurs at the same time as peak VGRFs. This is the link you are looking for, we think. Further, once this link has been determined, what variables one can determine to attenuate or increase this peak VGRFs.

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	study by Stacoff et al. (Stacoff et al., 1988) which showed that the knee joint angle can be used to reduce the magnitude of the impact loads during landing." .This sentence should be reworded since the results indicate that the 6 subjects did not need to increase knee flexion at maximum GRF for the test conditions, but they could have use knee flexion to reduce impact loads if required.	. We are simply reporting our findings for the six subjects tested. We never claimed that " bending the knee cannot be used as a strategy" instead we stated that "Our results showed that at increasing vertical heights, knee flexion was not correlated to peak VGRF and therefore may have little potential for reducing the risk of non-contact ACL injuries during single-leg landings." Incidentally this is supported by the literature.
	."However, our study is in agreement with findings of Faugenbaum et al. (Fagenbaum and Darling, 2003) who showed that factors other than knee flexion must significantly contribute to an increased risk of noncontact ACL injuries." .Since this study is not testing at an ACL injury level, the study results cannot be used to make a statement on increased risk of noncontact ACL injuries.	. If the subjects "could have used knee flexion to reduce impact loads if required" is unkown. We need to report what our data tells us. Our data show they did not, we are simply reporting our finding.
	."Moreover, it may be inferred from our findings that the ankle may not be effective for modulating peak VGRFs at increased height of jump." .I need to see the results across heights to evaluate this statement ."Our study also showed that at increasing vertical height, an increase in hip and trunk flexion	.Thank you for the comment. We believe this should have been discussed during the period of the student's studies.

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	can significantly reduce peak VGRF and subsequently reducing the risk of non-contact ACL injuries" .Your study showed that a negative correlation existed between hip and trunk flexion and jump height. Therefore, hip and trunk flexion angles were smaller at increased heights. This does not support the statement .Secondly, the study did not look at the effect of using more trunk and hip flexion at a higher height to reduce VGRF. You would have had to have subjects perform a series of jumps at the same high height but with progressively more hip or trunk flexion and the see the effect on VGRF. .Lastly, peak VGRF was not significantly reduced at the higher heights (i.e., higher height, greater VGRF)	.The paper was written with a specific objective. The additional info you seek is not required, but can be inferred quite clearly from data in table 2. . ANOVA analysis was first conducted to test the effect of height on GRFs, and then the effect of distance on GRFs. After running this analysis, if there is a significant effect then we move forward. In our case, we found significance and further ventured to investigate the association between GRFs and kinematics, knee power and knee work. The statement you quoted came from the second round of analysis; given first set of analysis revealed height is associated with peak VGRF. Now table 2 shows that hip and trunk flexion are negatively and significantly correlated to peak VGRF. Since we found a negative value for the correlation between hip and trunk flexion and peak VGRF, what this implies is an inverse association (large values of *X* tend to be associated with small values of *Y* and vice versa). . No, not quite as it would defeat the objective of the thesis. We did investigate more variables but the ones presented provided the greatest level of depth for study reporting and comparisons with the literature. The second state of analysis you are questioning was meant to determine whether the body kinematics, knee power or knee work can modulate the peak GRFs. If they can, then these variables do have a potential to reduce the risk of non-contact ACL injury. It is unclear to us as to what you are asking for. The first sentence of the results section states "As reported in Fig. 1, there is a relatively high positive correlation between vertical height of landing and peak VGRF (r=0.628, p=0.005)."

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81	.Page 97: ."Even though there are no single-leg landing studies to draw comparisons" .A large number of studies on single leg landing report joint angles, for many heights. These can be used for comparison. ."these findings are in agreement with the literature that reported that increased hip and trunk flexion may reduce the risk of non-contact ACL injuries" .The results do not support this statement ."Forward trunk lean and increase hip flexion may place the body COM more anterior and could potentially decrease the contraction demand for the knee extensor muscles (i.e. quadriceps muscles), while increasing the contraction demands for the hip extensors (i.e., hamstrings muscles)" .You reported a significant positive correlation for knee moments and powers, so the results do not support this statement about reducing demands at the knee. ."at increased distance of landing, our study found that there is a statistically significant relationship between peak PGRF and ankle and knee flexion,"	. The identical comment was raised at the thesis proposal in which several papers were presented as being identical (see attachment A). In addition, this comment was raised and addressed by the student at the thesis proposal stage. What was the outcome of this effort by the student and why is this question being asked again at this stage? At the thesis proposal a similar claim was made. See attachment A. ALL these papers were refuted and deemed irrelevant to the scope of our work at this time. It would have greatly constructive if you provided these references to demonstrate this. . Repeated comment. This comment was already made and addressed above. . Repeated comment. This was a mistake as reported earlier. The correction has been made to the tables. Text stay as it is given and it does state negative correlations between knee power and work and both peak VGRF and peak PGRF.

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	.The correlation between PGRF and angle flexion was not significant ."Our results corroborate these findings showing that by increasing ankle plantiflexion, there will be a reduction in peak PGRFs for landings performed at increased landing distance" .The results do not support this statement. PGRF is greater at longer distances. Since ankle dorsiflexion was defined as positive, the ankle was dorsiflexed at max PGRF. Also see previous statement about study methodology to verify this statement.	. Thanks for the point. Change has been made. . The fundamental challenge in describing joint angles is the desire to have both mathematical consistency between the descriptions of the different joints (e.g. all joint angles described using the same rules), and have anatomical meaning in the resulting signals. In Visual3D joint angles are simply the transformation from one segment coordinate system to another segment coordinate system. So if two segment coordinate systems are aligned perfectly (even though they may be displaced from each other) the resulting joint angle signal is zero. The ankle angle is a good example of the inconsistency between a general method for modeling (e.g. the segment coordinate system z-axis is aligned from the distal to the proximal end of a segment) and the ankle joint angle that would result from this definition. Using this standard definition, the ankle joint angle during standing would be approximately 70 degrees of dorsi-flexion, which is not the value most people want to see. To accommodate this inconsistency Visual 3D recommends that the user create a second virtual foot segment for which the alignment during the standing trial yields the desired joint angle. There are several ways of doing this, but two potential solutions will be described. We never did this. Instead we took the absolute value of the difference in joint angle between that when the subject was standing on the platform and that when the subject landed. .Thank you. The changes have been made on page 98. Table 2 clearly reveals that "by increasing ankle plantar flexion, there will be a reduction in peak

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	.“an increase in distance of landing led to a reduction in peak PGRF” .The results showed an increase in maximum PGRF with increasing distance (figure 2). Values are increasing negatively, due to the force plate axis convention.	PGRFs.” A table has been added to the thesis clarify this. . Thank you. This is an oversight, you are correct. The correction has been made on page 98 as follows: “an increase in distance of landing led to an increase in peak PGRF.” See page 98 with amendments.
82	.Page 98: .“Perhaps the answer can be found in the time to perform such tasks. For increasing landing heights the time to perform the single-leg landing is very short, perhaps to short to allow the muscles surrounding the ankle and knee to respond.” .No timing results were presented to support this statement. These results must be included in the paper. How much less time with increasing height? How does this difference relate to motor control times? .Which time are you referring to, from airborne to landing, from ground contact to maximum force?	. We could determine no reason to substantiate “why at increasing vertical heights of landing, the peak VGRF is poorly correlated to ankle and knee flexion and significantly correlated to both hip and trunk flexion?”. Barring the results of this study, we **speculate** that “Perhaps the answer can be found in the time to perform such tasks. For increasing landing heights the time to perform the single-leg landing is very short, perhaps too short to allow the muscles surrounding the ankle and knee to respond.” Please note that this is the discussion section of the paper. . We are referring to from takeoff to landing. .Valid point of view– thanks for the point raised here. Our point of view is that statement remains given in the discussion we wanted to talk around and

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	.without evidence, this statement should be removed.	rationalize our findings.
	."Future studies by the authors will endeavor to employ a larger sample size as well as to account for the effect of gender during single-leg landing from varying heights and distances." .This sentence is typically in the conclusions	.Thank you. It might be the case. But is reads and flows well with the limitations section of the discussion section.
	."The landing strategy recommended here and discussions stemming from this study" .A landing strategy was not recommended in the paper .No discussions from this study were reported	. The paper states: "Our results suggest that at increasing vertical heights, hip-trunk strategy seem to be used by the subjects, while for increasing distance, an ankle-knee strategy is used." . Need clarification and more explanation on this comment. Please provide us
	."Further in vivo and in vitro studies using a large and varied subject population, as well as computer simulation studies are needed to solidly validate our findings, and determine whether the landing strategy found actually reduces ACL loading in vivo." .This sentence can be removed since it is not related to the study (i.e., no ACL-injury inducing findings were reported in the study that would need to be validated)	.This exact comment was raised and addressed by the student at the thesis proposal stage. What was the outcome of this effort by the student and why is this question being asked again at this stage?. This sentence is valid. Removal of this sentence would implicate that the risk predictor variables i.e. peak VGRF and peak PGRF would have to be removed. The validity of using these two predictor variables hinges on what is known in the literature, which as you have stated here has not been proven. However, this as we have stated is a limitation of this study and most of studies of this nature. . How does one determine if a "study results are successfully related to prior studies". Given the lack of consensus and agreement in the

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	."This study investigated the relationships between varying vertical height, horizontal distance, and peak GRFs during single-leg landing and further related these findings to risk of non-contact ACL injury" .The study results were not successfully related to ACL injury	literature as this thesis highlights, this study first reinforces earlier studies of similar nature, but more importantly it adds to the literature the aspect of how the body can modulate knee loads from increasing heights and distances, which is absent from the literature. As well, the author has related his findings to risk of non-contact ACL injury (a domain on its own) which in itself is a contribution.
83	.Page 99: ."Further, at increase height of landing, hip and trunk flexion may be more appropriate for attenuating GRFs" .This statement is not supported by the results .More appropriate that what other strategy? ."while at increase distance of landing, ankle and knee flexion may have more potential to attenuate GRFs" .This statement is not supported by the results .More potential that what other strategy? ."Hence, the biomechanical strategies for decelerating the body in the vertical and horizontal directions may be different." .You can make a stronger statement	. Table 2 shows a negative and significant correlation between both hip and trunk flexion and peak VGRFs. This implies a negative association. Therefore, a high hip and trunk flexion results in lower peak VGRFs. Hence, the statement seems correct to us. The claim of GRFs is misleading and the results do not show this. To be exact this should state peak VGRFs as our results reveal. Change has been made on Page 99. . Note one of the claims made by other reviewers is that ankle flexion at p=0.104 is not significant. Given there were oversights in the way ankle flexion was calculated upon reanalysis, it is thought that this data is greatly significant. . More appropriate has been reworded on Page 99 to avoid any confusion. . See statement above as same argument applies. . We have reworded this statement in the discussion and have moved it up to the abstract to strengthen our argument. Change has been made on page 99 and in the abstract of this paper.

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	since, for your subjects, there was a clear difference between vertical and horizontal landing strategies ."In addition, both eccentric knee power and eccentric knee work was positively and significantly correlated to both peak VGRF and peak PGRF" .PGRF knee work was not significantly correlated	. Thank you the change has been made on page 100.
83	Text edits .Page 104: "explain the higher number of injuries among females"	. Change has been made on page 104.
84	.Page 106: "To undertake this, a relationship between three non-contact ACL injury risk predictor variables (maximum VGRF, maximum PGRF, maximum knee abduction moment) and selected single-leg landing biomechanical variables were studied"	. Change has been made on page 107.
85	.Page 107: "The seven camera motion capture system (Vicon MX, Oxford Metrics, UK) collected marker trajectories at a sampling rate of 250 Hz."	.Change has been made on 108.
86	.Page 111: ."F(1,9)=20.91, p<0.01, partial η 2=0.699 with ankle plantar flexion	. Repeat of previous comments.

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	angles." ."More specifically, there was a significant height×distance interaction Greenhouse-Geisser adjusted" ."interaction Greenhouse-Geisser adjusted F(3.31, 29.79) =3.73, p=0.019; partial η 2=0.293 for peak VGRF, F(2.17, 19.54) =4.13, p=0.029; partial η 2=0.315 for knee internal rotational moment, F(2.58, 112 23.22)=3.15, p=0.05, η 2=0.26 for hip flexion, and F(2.98, 26.79)=3.90, p=0.02, η 2=0.30 for trunk flexion." .This sentence is difficult to read. Please revise.	. Height mis-spelt change has been made on Page 112. Change has been made on page 112-113.
87	.Page 104: ."The number of non-contact ACL injuries is higher among females; however, there is no conclusive evidence that this is due to biomechanical differences between genders. One explanation is the lack of studies investigating gender differences in whole body biomechanics during single-leg landings from increasing vertical heights and horizontal distances." .The evidence is strong that males and females have biomechanical differences for the target activity related to landing (many studies,	. Comment repeated. See Attachment A. This was raised and addressed by the student at the thesis proposal stage. Further, please share with us the studies that determined these biomechanical differences explains the gender disparity in ACL injury rate. Please note that as stated clearly throughout this thesis, the focus of our work is just on single-leg landing.

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	some with large samples). The statement should be revised ."reaction force (PGRF) for males (r=-0.85, p=0.004)," .Assuming that the 6 males are the same people as in paper 4, why is the r value different?	. Please recognize that the *r* and *p* values in paper 3 were revised (See page 96) and also take note that paper 3 jump tasks studied are different from paper 4.
88	.Page 105: ."while nearly significant and moderately correlated to peak PGRF for females (r=-0.542, p=0.13)" .0.13 is not nearly significant at the p<0.05 level ."while no significant interaction was observed for distance and gender" .Why would you anticipate an effect for distance and gender? Both gender group performed the same methods and therefore move the same distance. .What are "ankle plantiflexion angle gender effects" ."There are few single-leg landing studies in the literature" .Many single-leg landing studies are in the literature, I made a quick search and found over 16 studies so far in 2011. The review paper by Schmitz, 2007 has 34	. The sentence has been revised on page 106. . This statement was made for completeness to explain all the interactions studied. . Ankle platarflexion was the only variable found to be significantly different between genders. This statement endeavors to capture this point. . Comment repeated many times. See Attachment A. A quick search on the internet is quite different than a thorough review of the content of these papers to determine its similarities or differences to this work. . See Attachment A. Please review the content of these papers prior to making this claim. If you believe there is merit to your claims, then do send us these studies. Further as a member of the thesis committee why you are raising this point now?- we are just wondering why?

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	references just on the topic of gender differences ."Further, most single-leg landing studies only report data on the knee joint kinematics and kinetics." .A sufficient number of studies report results for other joint, therefore this sentence should be revised ."Hence, peak PGRF may also predict the risk of sustaining a non-contact ACL injury" .Alternatively, it may be the increased in resultant force that is the issue and not an isolated increased in the PGRF vector. Greater VGRF also causes an increase in eccentric knee extensor moments.	. Please provide the study that supports this statement. . This statement is based on what findings or studies- it's not clear to us. We are likely to find a study in the biomechanics field that states the exact opposite.
89	Page 107: .Please make same changes to Procedures as outlined in the Paper 3 comments	. Thank you. The requested changes have been made in the thesis.

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90	.Page 109: ."ACL injury risk predictor variables and various selected dependent variables" .Please list the variables ."current study did not produce the characteristics distinct biomodal GRFscurve commonly reported during double-leg landing (Dufek and Bates, 1990; Zhang et al., 2000)" .The GRF curves were consistent with single leg landing curves form the literature. The sentence should be revised to compare with single leg landing and not double leg landing, since this is a single leg landing study. .This sentence should also be moved to the discussion since a literature comparison is not needed in the results. ."The demands of the current tasks studied resulted in a smoother increase to GRF" .Smoother than what? ."Therefore, the biomechanical comparisons of double leg landing with single leg landing results in the literature may be limited due to the differences exhibited by the two tasks."	They are too many to list. These variables are clearly labeled and listed in table 1. . This statement is important to the paper and will not be revised. It has now become more apparent why many of your previous comments were made. This is indeed a single-leg landing study and the impetus of making this very simple statement and presenting the first two figures of this paper is to clearly highlight that single-leg landing biomechanics is different from double leg landing biomechanics. .Thanks for your comment. Change has been made on page 110 and 115. . Word change to smooth on page 116. . The statement is valid as it explains why one cannot compare results from double-leg landing with single leg landing. It also explains why there is a lack of data to aid comparison with those in the literature. Finally, it helps one understands that this is the first and only study in the literature investigate the effect of increasing vertical height and horizontal distance during single-leg landing with results related to ACL injury.

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	.Comparing single and double leg landing is not the focus of this paper, so these sentences should be removed.	
91	.Page 111: ."Follow up tests with the three non-contact ACL injury risk predictor variables" .No follow-up tests were described in the methods ."Females had significantly less ankle plantiflexion angle than males" .What stats were used for this result? ."while a moderate but near significant negative correlation for females (r=-0.542, p=0.131)" .0.131 is not near significant at the p<0.05 level	. We have added details to better address your comment. . Please see table 1 that illustrates only ankle plantarflexion was significantly different between genders and the magnitude of this difference is shown in table 2. . Wording has been changed to: "while a moderate but not significant negative correlation for females (r=-0.542, p=0.131)"
92	.Page 112: .Table 2 must provide mean and SD for all outcomes discussed in the results and discussion.	. Please provide us with more details. What exactly is being discussed in the results or discussion section for which data is not presented. The flow of this paper follows a systematic approach. This approach is built with table 1 as the focus. First gender effects are discussed with all necessary data. Given only ankle plantarflexion was different between genders males' and females' data were pooled. From here interaction are studied and then main effects.
93	.Pages 113-114: .Table 2: The results for males are	

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	strange since the ankle is more plantarflexed as the height increases but dorsiflexed (or less plantarflexed) at the longer horizontal distances. This typically means that the tibia is behind the ankle when the foot is flat (assuming maximum VGRF does not occur until the heel contacts the ground). Since the knee is approx. 28-32 degrees flexed and trunk is 17-21 deg flexed, this puts the body in a strange position (see below). The dorsiflexed ankle angle for the women seems more understandable.	. Height has no significant impact on ankle plantarflexion angle. See table 1. This is even more reinforced by looking at the data in table 2. We have looked at the data again in visual 3D and the values obtained from males are what we have reported.
	.As in the figure below, cofg would be behind the base of support and without arm motion recovery of balance would be difficult	. This point is repeated. See above comment for details. One standardizes arm location to reduce variability. Variability can be high in human motion and can prevent one from predicting anything significant. Strict experimental controls will likely introduce other limitations and traded one confounding variable for another. Further, this should have been provided to the student at the thesis proposal stage. This comment was repeated many times so far. Qualitatively only females had trouble with balance especially at the higher heights. The issue of location of body COM with respect to base of support is discussed later on in the paper.
	.Since the SD for ankle angles are quite high (1-5x higher than the mean) does outlier data account for	.Thanks for your comment. This is a very good point. When we looked at the scatter plots of each subject over the various landing configuration, no obvious outliers were noticed. See Attachment F that shows the scatter plot for a male and a female subject. What this figure reveals is that there is an almost linear increase of ankle flexion at each height as distance increases. Further, the Z scores provided (See attachment G) of angle flexion angle for all subjects at all levels were calculated. The Z scores are provided in Attachment G. For the case of ankle flexion angle, no

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	these differences? . This should be discussed	outliers. For the case of knee, hip, trunk flexion, no outliers. . We think that you must be referring to ankle plantarflexion and PPGRF with this question. Please note that this correlation was corrected in Paper 3. Secondly as mentioned above, the tasks performed in Paper 3 and Paper 4 are different.
	. Table 3: Why are the correlations for males greater than in paper 3?	. Yes, all trials across all conditions for each subject were used. In paper 3, not all conditions were tested. Table 5 is for all conditions and all subjects.
	. Are all trials across all conditions used for these correlations? . Table 5: Are these correlations for all conditions and all subjects? . Data are duplicated in tables 5 and 7	. For ease of readership, this was done given the systematic approached used by the paper. Given there are 4 variables that are significantly impacted by height x distance interactions, first the means and SDs are presented (see table 4) and then these four variables are correlated to the three possible ACL injury risk predictor variables (see table 5). Table 6 and table 7 follow the identical approach, but presents only the main effects of height and distance. So, given VGRF is impacted by both height x distance interactions and main effect of height, it is presented in both tables. Note that change was made throughout to correct this and to prevent duplication of data in tables.
94	. Page 115: . See ankle angle comments above . "Our results revealed that females exhibited significantly lower ankle plantiflexion" . Females are dorsiflexed (Table 2) . "which offers a possible explanation	. See Attachment A. See comment above. . This is correct. The word plantiflexion was removed. Change made on Page 116. . Agreed but these studies do show that ankle plantiflexion angles have the potential to modulate the GRFs. Please keep in mind that the time

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	to the higher number of non-contact ACL injuries among females," . Since you are analyzing the ankle angle at maximum VGRF, this point does not relate to the mentioned studies, which are considering ankle angle at initial contact . "Hence, a reduction in peak PGRF may be realized by increasing ankle plantiflexion during single-leg landing which subsequently may reduce the risk of non-contact ACL injury" . PGRF did not decrease as distance increased, so this point is not supported. . "Perhaps an increase in plantiflexion permits more time to distribute the impact forces and better enables the musculature to absorb these forces as demonstrated by the following studies" . This study only looked at the maximum VGRF instance in time so this statement is not supported by the study. . "and implies that horizontal distance of landing--often ignored in most studies--is an important variable"	between initial contact and peak VGRF is short. What our finding shows is that ankle plantar flexion is significantly different between genders and that this difference may offer a possible explanation to disparity is ACL injury rate. . Changes have been made throughout page 116 to clear the confusion with ankle plantiflexion versus dorsiflexion. . This comment was repeated. When you say "this study" we assume that you are referring to this thesis. If this is the case, what this statement is aiming to do is to substantiate our findings with that in the literature. . We cannot understand your comment. We never mentioned anything about force components in this sentence. Please clarify. . Horizontal distance is important. Distance should be considered in future single-leg jump landing studies. We are not quite sure what you are saying. . You failed to include the complete sentence in this quote. "Our results also suggest that knee abduction moment can be modulated by increasing trunk flexion

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	.This force component is not ignored, please rephrase .Importance for what? ACL indicator? I would expect that the resultant force is the main item, with this force being larger if the person jumps farther (higher, longer, or longer and higher) ."Our results also suggest that knee abduction moment can be modulated by increasing trunk flexion" .This statement how you arrived at this statement. Please expand on this and support with the project outcomes. ."Given there are no single-leg landing studies to draw comparisons" .Many single leg landing studies exist for comparison. Please use these.	(see Table 5)." So table 5 is how we arrived at this statement. . This comment is repeated several times see responses above. . We will address the ones you have mentioned. H=height D=Distance . The peak VGRF increased with H and D (see table 6). Knee flexion angle decreased with increasing H (see table 6). Hip abduction angle decreases with increased H and D. Therefore, a negative correlation is reported as per analysis done using SPSS. A negative correlation implies an inverse association. What this means is an increase in X leads to decrease in Y and vice versa. Therefore, the statement with regards to knee flexion angle, that is, increase knee flexion angle is associated with reduced peak VGRFs is correct. We check all other variables you have mentioned and this statement is correct. Further, a positive correlation implies small values of X results in small values of Y, and large values of X are associated with large values of Y. So for example the vertical distance between foot center and body COM increases as H increases. As mentioned already, peak VGRF also increases with increase H. Therefore, positive correlation which implies small values of peak VGRFs is associated with small values of vertical distance between foot and body COM. . This comment was repeated several times. H=height

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	. "Perusal of the main effects of height and distance correlated with selected biomechanical variables (see table 7) revealed that increased knee flexion angle, hip abduction angle, knee power, knee work and horizontal distance between foot and the body COM, as well as, an accompanying decrease in vertical distance between foot and the body COM, is associated with reduction in peak VGRF, thereby demonstrating the possibility of these variables to reduce the risk of non-contact ACL injury. .This statement has many problems. .VGRF increased (i.e., not reduced) .Variables increased as VGRF increased, so how can you prove that these variables reduced risk (i.e., variables increased but VGRF still increased) . "Without studies to draw comparisons" .Other single landing studies exists that can be used for comparison . "In addition, our results revealed	D=distance . peak PGRF increases with increasing H and peak PGRF decreases with increased D (see table 6). Since Knee flexion decreases with increase H, this implies a negative correlation. Checking all the other variables used revealed that this statement is correct. . This is your opinion, which we respect, but our data from this study by no means support this. We have formulated our discussion and conclusions on the findings of the paper. Q angles were not within the scope of this study. . We do not know why females injure their ACL more than males. We both however may agree that there is a difference in average varus/valgus between males and females. Therefore, for the same applied external load, for example during landing, will require different muscle actions to maintain internal equilibrium. The authors of the following papers did just that for single-leg landings (Lawrence RK, Clin. Biomech. 23,6,2008; Nagano Y. et al., The Knee, 14, 2007; and Russel KA, et al., J. Athl. Training, 14,2,2006) and for double-leg landing (Decker MJ et al. Clin. Biomech. 18,7, 2003, Kernosek TW, Med.Sci. Sports Ex. 37,6, 2006, Chappel JD, Am. J. Sports. Med, 30, 2, 2002). Given the distal femur is inherently adducted one might argue that even with a sagittal plane dominant movement like that studied in this thesis, to counter the large loads knee abduction moment may be required. Hence, some subjects may possess larger frontal plane deviations that may likely be countered

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	that at increased in plantiflexion angle, knee flexion angle, knee power, knee work, and horizontal distance between foot and the body COM, as well as, an accompanying decrease in vertical distance between foot and the body COM is associated with a reduction in peak PGRF. .Same issues as with VGRF .PGRF either increased with greater horizontal distances or was almost unchanged (h60d30,h56d50) ."knee abduction moment and the biomechanical variables tested suggesting that knee abduction moment may be less a predictor of risk of non-contact ACL injury compared to peak VGRF and peak PGRF for single-leg landing tasks." .This may be due to the female subject sample for the study. Did the subjects have moderate-large q-angles? .If the subjects did not land in an abnormal knee abducted position, then you cannot test to see if knee abduction moment is a good indicator since the moments would be larger if the person lands with more knee abduction.	with the abduction moment. Given this, the merit of reporting and studying this variable even for a sagittal plane dominant motion is interesting. Note as well please that the international Olympic committee current concepts statement (Renstrom P. et al. Br. J. Sports Med., 42,6,2008) shows that "a combination of anterior tibial translation (ATT) and lower extremity valgus are probably important components of the mechanism of injury in athletes." . We do agree that some people may have frontal plane deviations. . Firstly, this comment contradicts an early comment made on accuracy with regards to values such as tibial rotation. The body center of mass is calculated in Visual 3d, so it is the foot center. For most if not all calibration done with the Vicon system, the mean residual was 1mm or under 1 mm, so one can argue that the range of 30mm is satisfactory. However, we are eager to know how you established that 3cm is within the error of identifying body COM. It is our view that the body position with respect to the BOS may give some global body (whole body) indication of risk of ACL injury given this value to date assesses balance. Given we know that an object with a lower COM is more stable, we were keen to determine how subjects used this to attenuate GRFs and stabilize their body. As well, for dynamics stability the position of body COM in relation to the BOS influences the body's stability. Given the large mechanical moment arm from body center of mass in relation to the BOS and the body's small BOS when the entire body mass has to be balanced on single leg during landing, the body's COM movement may significantly influence the loads seen at the joint especially more so when the COM is posterior to the BOS. As an example, upon landing, the literature suggests that to modulate the GRF a forward trunk lean may be useful (Blackburn and Padua Clin Biomech, 2008, Olsén et al AJSM 2004). . All subjects start the jump task from a standard position on two legs,

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	.Your subjects may have been sagittal plane dominant but some people have larger frontal plane deviations (see literature on females landing)	move to dominant leg and then jump. Given the point of interest at which vertical distance was determine was also standardize we used this to establish globally what the entire body was doing. We wanted to see how vertically collapsed/crushed subjects were and how much this attenuated the GRFs. Interestingly, as a strong positive correlation was determined and further showed from a whole body perspective lowering the body COM can reduce the VGRFs. To date this is a value seldom reported in the literature, but perhaps one to foster more debate in the future.
	."Our findings (see table 7) reveal a significant and high positive correlation between both peak VGRF and peak PGRF, and the vertical distance between the foot and body COM supporting the findings in the literature …".	. This comment was repeated several times, please see our responses above. . Please read the entire sentence. The authors accept that the small sample size is a limitation of this study. Given from initial tests conducted in the lab it appeared that trials were similar and given this, it was also decided that a small sample size was ok.
	.The COM results are for vertical COM distance should be discounted since this distance only changed by 3 cm (96-99 cm) and this difference is within the error of identifying COM. Therefore, the data shows that vertical COM could have no real-world effect, even through there was a correlation.	. Thank you. The sentence has been reworded to remove the phase landing strategy recommended. Please see Page 118 . This has been amended on Page 119.
	.Also, you did not measure the range of COM motion so the study cannot show if COM was lowered.	
	."Due to the lack of studies	

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	examining body kinematics and kinetics over increasing heights and distances, we are unable to fully compare our results with the literature." .If you make a table with the results from the literature, you will have information for many variables over a range of heights and distances, for many subjects. ."relatively small sample size (N=11)," .Comparison size is even smaller (n=5 for females) ."The landing strategy recommended and discussions stemming from this study" .See paper 3 ."Lower plantiflexion angles was observed for females" .Females were dorsiflexed, which will allow the ankle to progress forward to attenuate forces. The problem would be if they landed with 0 degrees and no movement occurred.	
95	.Page 122: "While contributing to an understanding"	. Change made on page 123.
96	.Page 128: ."uses the anthropometric data measured for each subject to scale	.We think that no change is required.

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	the MSM (Rasmussen, 2005). An optimization-based method …" ."taken, firstly, we compared" ."This information is presented in an on-off timing curve (Fig. 2) that shows when the measured and predicted muscles activity goes above (turns on) and below (turns off) a 20% threshold during single-leg landing. Secondly, …"	. Change has been made on page 128. . Change has been made on page 128.
97	.Page 129: "using the subject-specific MSM, example provided in Fig. 3, after completing"	. Change has been made on page 130.
98	.Page 131: "Separate 3×3 two-within-one-between subject repeated measures ANOVAs were conducted"	. Change has been made on page 132.
99	.Page 122: ."Results revealed no significant gender differences in the musculoskeletal variables tested except peak VGRF (p=0.039), as well as, knee and hip axial compressive force (p=0.05, and p=0.032, respectively)." .In paper 4 no significant difference was found for VGRF but the 3 subjects that were selected for paper 5 show a significant difference. Therefore, the selection of these 6 subjects is questionable.	. The 6 subjects used for this paper are a subset of the subjects used in paper 4, but there were height and weight match as far as possible. We re-did the stats to test the effect of gender on VGRFs and the results reported in paper 5 are correct (See attachment B). We also re-did the stats on paper 4 to make the same inquiry and the results reported for paper 4 are also correct (see Attachment C) The only small issue we can see is as follows: 1. The filter used to smooth the analog signal for visual 3D and AnyBody were a bit different. But, given all the data went through the identical filter process, we know this should have no effect on the test for variances. Regardless, the rationalizing why this is the case fails us at this time. . Nothing special was done to select subject from the population except

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	.Since axial load is related to VGRF, these significant differences could also be attributed to subject selection from your population sample.	that they be height and weight match as closely as possible. We would really like to know how you have determined that "axial load is related to VGRF". How is it related? Please share with us the mathematical relationship that captures this relation? We are eager to know and learn from you.
100	."Our results showed no significant association between quadriceps force and risk of ACL injury" .This makes sense since you did not have injury inducing loads during testing ."Within the limitations of the subject-specific MSMs, our findings indicate that musculoskeletal variables studied are not the sole determinants to ACL injury." .It is difficult to make a statement on ACL injury based on the methodology	. This comment was repeated many times. Please see above for response. The identical comment was raised at the thesis proposal in which several papers were presented as being identical (see attachment A). What are the loads to induce injury to the ACL during implicated injury mechanisms? This data does not exist in the scientific community. We do have *in-vitro* data and using this data we can all agree that the experimental protocol used here exceeded the load to failure limits of the ACL. Now the question is why did the ACL did not fail? The answer perhaps lies in the body kinematics as well as the active response of muscles to attenuate these loads during landing. . Why is it difficult? Please let us know what methodology or approach would you suggest to study risk of ACL injury during sport movements? If your statement had any validity, it would invalidate the thousands of experimental *in-vitro* and computational modeling studies in the scholarly literature in the domain of non-contact ACL injury.
101	.Page 124: .Check references for Shin (2007,2009, 2011), Mokhjtarzadeh, Yeow, et al. (2010), Bulluck (2010 - Masters Thesis) for models and single leg landing .Since loads at 60 cm are non-injury inducing but higher than the	. Thank you for the references. Shin's research group work is based on a finite element model, which is quite different from a musculoskeletal model (see paper 1 for differences). . Mokhjtarzadeh, Yeow, et al. (2010) work was published in a conference proceeding. . Work of Yeow' research group was referenced in the thesis and used for comparisons. Note that the scope and test protocol for Yeow's research group work

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	lower heights, are the lower height trials necessary if the focus is on ACL injury? .Bulluck performed a similar study so his results should be used in the comparison. Especially since quadriceps and hamstring results were different. ."The ability of body kinematics or lower extremity muscles to attenuate the GRFs upon landing from a single-leg requires further investigation." .This broad statement is not supported. Many studies exist in the literature, what aspect of force attenuation is lacking? .What do you mean by "elaborate internal joint loads"?	is not the same as ours, e.g. barefoot landing. .Could not find anything on Bullock. The identical comment was raised at the thesis proposal in which several papers were presented as being identical (see attachment A). How did you establish that the loads at 20 cm or 60 cm are non-injury inducing. Kindly provide us the study(s) that shows this. We are eager to learn. The three heights were used to provide three data points that would enable one to study trends. Two data points will always result in a linear relationship. . We would be glad to look into this reference to assess its merit for inclusion in this work. . Comment repeated several times. Please see our responses above. See attachment A. Change has been made on page 125
102	.Page 125: .Weight and height matching of the males and female populations does not necessarily improve the methods since females are typically shorter and lighter than males. .What shoes were worn (brand, etc.)	. Weight and height matching was not done to improve the method. It was used to reduce the variability in results caused by BMI. BMI has been implicated as a contributor to risk of ACL injury. . Thank you. Change has been made on Page 126.
103	.Page 128:	. Change has been made on Page 124

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	.Define AMS .IDA is not used later in the text so this abbreviation can be removed ."Secondly, the joint forces and moments measured in vivo at the knee joint during gait and reported in the literature were compared with predicted knee joint forces and moments" .Include reference to this gait literature. Was this walking gait? Both males and females? .This paragraph can be rewritten to more clearly show the methods. For example, ."Secondly, the joint forces and moments measured in vivo at the knee joint during gait and reported in the literature were compared with predicted knee joint forces and moments (Table 1). The MSMs were driven with the individual subject's knee joint forces and moments obtained from single leg drop landing trials. "Based on these findings and recognizing variability in body anthropometry between studies, it appears that the developed subject-specific MSMs tends to .reproduce the trends in internal	. The resubmitted manuscript uses this acronym more than once so no change required. . Change has been made on Page 129. .Yes, walking gait. .Yes, both males and females . Thank you for the suggestion offered. We feel the text reads well given the MSMs are not driven with the individual subject's knee joint forces and moments obtained from single leg drop landing trials.

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	forces and moments well while systematically overestimating the joint reaction forces." .Which findings? The literature review? .No trend for most measures in table 1 (i.e., only one comparison value) .Anybody results are higher than the range for Fz and Fx only, therefore they do not reproduce the trends and did not show a systematic overestimation (Fy was not higher) .What are the Anybody results? Mean of all 6 subjects? ."The latter can be controlled in the MSMs by adjustment of muscle moment arms, but in the interest of reproducibility it was elected to not pursue this option." ▪What is "the latter"? ▪ So what was done to correct the models? Was the error left in place?	. We are referring to the outputs from the MSMs . Change has been made on Page 130. . Change has been made on Page 130 . The moments at the joints are primarily what are used to balance internal loads with externally applied loads. These moments as shown in table 1 are well within the *in vivo* data from the literature. The joint reaction force, Fy, is very nicely within the magnitude of *in vivo* data from the literature. . Anybody results are provide in table 1 second column labeled "predicted by AnyBody MSM". The data for the MSM is for a single subject. This subject was our heaviest subject given the body weight of subjects available in the literature. . The latter refers to the overestimation in joint reaction forces. . What correction you feel is warranted. Further, what error you speak of. A model is a representation of reality and in no means a way to directly compare with the human body. It is simply an order of magnitude comparison.
104	.Page 128: ."The time at which peak VGRF occurred was used to determine the selected musculoskeletal variables."	. This sentence is correct.

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	.This sentence indicates that the VGRF time in seconds was used to select the variables used in the analysis. Since this is probably not the case, please revise.	
105	Page 130: Figure 2: .The activity and start-end events are unclear. .Including event timing in the figure would help the reader (foot strike, etc.).	. We do not see the value in adding events at a threshold of 20%. At this threshold only initial contact may be worth reporting.
106	.Page 132: ."Nonetheless, the trends in the predicted muscle activations (thin lines) sets in reasonably close in time as the measured muscle activations (fat lines), therefore demonstrating fairly good agreement between model prediction and experimental data" .What do you mean be trends? .The comments of "reasonably close" and fairly good" do not support the use of the defined model for further study. Tibialis anterior and rectus femoris are quite different and the timing/duration factors could adversely affect the model's ability to predict forces.	. By trends we mean the period of time and length of time the predicted muscle activity is over the 20% threshold. . Naturally this would be the case for any computational model given the state of science to date. Aiming for anything that is more than an order of magnitude comparison is not realistic. Please let us know how would "the time/duration factors adversely affect the model's ability to predict forces?" and How does one address this in the muscle model?

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	.It is not clear where Figure 3 shows the interaction with the environment	. Thank you. This has been corrected on Page 133.
107	.Page 133: .Figure 3: It is questionable to state that the model has been validated due to the errors.	. Model validation is a great discourse in the field of biomechanics and is a place where anyone can easily attack. Please consult the on-off timing curves provided on for model validation. For the most part, this is the gold standard for MSM validation if validation is done in the study. We have done this and to further acquire confidence in our model we compared our model predictions to *in-vivo* data from the literature. Model validation requires experimental data to facilitate validation. In many cases, like ours, such data is difficult to obtain, or may never be obtained. The validation in this thesis is to show the model outputs reasonable trends for joint reaction and muscle activation. In general, ALL musculoskeletal models overestimates the internal forces. It seems that everyone in the musculoskeletal modeling community will agree that ALL MSMs yields larger joint forces than they would expect. We will be keen to understand what threshold of error warrants a MSM model valid in the field of biomechanics. Further, please be aware that for the *in-vivo* studies all subjects were heavier (i.e. ~335 N heavier than the heaviest subject in our study). To date, no data exist for subjects within our body weight.
	.A table of means and SD for main measures is required (maximum VGRF, Hip & Knee axial forces, max PGRF, max Proximal tibial shear force, etc.), with male and female results separated.	. The table of the dependent variables that are significantly different between genders have been added on page 135.
	.Later in the document, Table 3 provided some data, but only for the entire sample. The male and female results are needed separately since this is the analysis that is presented.	. See comment above please.

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	."Between genders, females had significantly lower peak VGRF, as well as, knee and hip axial compressive forces." .What statistic was used for this post hoc analysis?	. Multiple 3 way mixed design with repeated measures ANOVA was used.
108	.Page 134: .Figure 4 .Revised to only show the data from foot strike onwards (inactivity from 8-85% is not needed for these graphs). .Y-axis scaling should be the same for males and females .In a printed version, I cannot distinguish the curves by the legend. PDF enlargement to 300% was sufficient.	. Revisions has been made on pages 135 and 136. See Attachment D and E. . Revisions has been made on pages 135 and 136 See Attachment D and E. . The figures are presented to show the trend in the data.
109	.Page 135: ."From descriptive statistics -not presented- one can observe an almost linear increase" .Since these statistics were not presented, I cannot observe this increase. ."Follow up test with this variable and the two non-contact ACL injury risk predictor variables revealed no significant correlation." .What was this followup-test. Please provide the methods and	. Please take a closer look at Figure 5a. . Change made on page 132.

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	results or remove from the paper. .Is height the jump height or the subject's height? ."Results revealed no significant height×gender, height×distance or height×distance×gender interactions (Table 1). .Table number is incorrect in paragraph	. We assume that you are referring to Table 2. In this table, we are referring to jump height. .Change has been made.
110	.Page 137 .Figure 5: The y-axis label is muscle force; however, the EMG data was not scaled to force but to a % of maximum voltage. How did these data become converted to BW?	. Figure 5 are outputs from the MSMs.
111	.Page 138: ."This study showed that single-leg landings did not produce the characteristic bimodal VGRF curve commonly reported for double-leg landings" .Yeow (2010) had similar shaped curves in his study that tested both single and double leg landing. .The reason could be that you did not allow arm movement on landing. Therefore you are correct that the difference was related to the task but it should be mentioned that you are dealing with a "single leg	. Thanks for your points. What you have highlighted simply reinforces our findings. Yeow's (2010) work was referenced throughout this thesis. . This comment is repeated many times. Please see responses above.